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(54) Title: CORYNEBACTERIUM GLUTAMICUM GENES ENCODING METABOLIC PATHWAY PROTEINS

(57) Abstract: Isolated nucleic acid molecules, designated MP nucleic acid molecules, which encode novel MP proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing MP nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated MP proteins, mutated MP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of MP genes in this organism.

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***CORYNEBACTERIUM GLUTAMICUM* GENES ENCODING METABOLIC
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Related Applications

The present application claims priority to prior filed U.S. Provisional Patent
5 Application Serial No. 60/141031, filed June 25, 1999, U.S. Provisional Patent
Application Serial No. 60/142101, filed July 2, 1999, U.S. Provisional Patent
Application Serial No. 60/148613, filed August 12, 1999, and also to U.S. Provisional
Patent Application Serial No. 60/187970, filed March 9, 2000. The present application
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8, 1999, German Patent Application No. 19931443.8, filed July 8, 1999, German Patent
Application No. 19931453.5, filed July 8, 1999, German Patent Application No.
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8, 1999, German Patent Application No. 19931478.0, filed July 8, 1999, German Patent
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19931541.8, filed July 8, 1999, German Patent Application No. 19931573.6, filed July
8, 1999, German Patent Application No. 19931592.2, filed July 8, 1999, German Patent
Application No. 19931632.5, filed July 8, 1999, German Patent Application No.
19931634.1, filed July 8, 1999, German Patent Application No. 19931636.8, filed July
25 8, 1999, German Patent Application No. 19932125.6, filed July 9, 1999, German Patent
Application No. 19932126.4, filed July 9, 1999, German Patent Application No.
19932130.2, filed July 9, 1999, German Patent Application No. 19932186.8, filed July
9, 1999, German Patent Application No. 19932206.6, filed July 9, 1999, German Patent
Application No. 19932227.9, filed July 9, 1999, German Patent Application No.
30 19932228.7, filed July 9, 1999, German Patent Application No. 19932229.5, filed July
9, 1999, German Patent Application No. 19932230.9, filed July 9, 1999, German Patent
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19932926.5, filed July 14, 1999, German Patent Application No. 19932928.1, filed July 14, 1999, German Patent Application No. 19933004.2, filed July 14, 1999, German Patent Application No. 19933005.0, filed July 14, 1999, German Patent Application No. 19933006.9, filed July 14, 1999, German Patent Application No. 19940764.9, filed August 27, 1999, German Patent Application No. 19940765.7, filed August 27, 1999, German Patent Application No. 19940766.5, filed August 27, 1999, German Patent Application No. 19940832.7, filed August 27, 1999, German Patent Application No. 19941378.9, filed August 31, 1999, German Patent Application No. 19941379.7, filed August 31, 1999, German Patent Application No. 19941380.0, filed August 31, 1999, German Patent Application No. 19941394.0, filed August 31, 1999, German Patent Application No. 19941396.7, filed August 31, 1999, German Patent Application No. 19942076.9, filed September 3, 1999, German Patent Application No. 19942077.7, filed September 3, 1999, German Patent Application No. 19942079.3, filed September 3, 1999, German Patent Application No. 19942086.6, filed September 3, 1999, German Patent Application No. 19942087.4, filed September 3, 1999, German Patent Application No. 19942088.2, filed September 3, 1999, German Patent Application No. 19942095.5, filed September 3, 1999, German Patent Application No. 19942124.2, filed September 3, 1999, and German Patent Application No. 19942129.3, filed September 3, 1999. The entire contents of all of the aforementioned applications are hereby expressly incorporated herein by this reference.

Background of the Invention

Certain products and by-products of naturally-occurring metabolic processes in cells have utility in a wide array of industries, including the food, feed, cosmetics, and pharmaceutical industries. These molecules, collectively termed 'fine chemicals', include organic acids, both proteinogenic and non-proteinogenic amino acids, nucleotides and nucleosides, lipids and fatty acids, diols, carbohydrates, aromatic compounds, vitamins and cofactors, and enzymes. Their production is most conveniently performed through large-scale culture of bacteria developed to produce and secrete large quantities of a particular desired molecule. One particularly useful organism for this purpose is *Corynebacterium glutamicum*, a gram positive, nonpathogenic bacterium. Through strain selection, a number of mutant strains have

been developed which produce an array of desirable compounds. However, selection of strains improved for the production of a particular molecule is a time-consuming and difficult process.

5 Summary of the Invention

The invention provides novel bacterial nucleic acid molecules which have a variety of uses. These uses include the identification of microorganisms which can be used to produce fine chemicals, the modulation of fine chemical production in *C. glutamicum* or related bacteria, the typing or identification of *C. glutamicum* or related
10 bacteria, as reference points for mapping the *C. glutamicum* genome, and as markers for transformation. These novel nucleic acid molecules encode proteins, referred to herein as metabolic pathway (MP) proteins.

C. glutamicum is a gram positive, aerobic bacterium which is commonly used in industry for the large-scale production of a variety of fine chemicals, and also for the
15 degradation of hydrocarbons (such as in petroleum spills) and for the oxidation of terpenoids. The MP nucleic acid molecules of the invention, therefore, can be used to identify microorganisms which can be used to produce fine chemicals, *e.g.*, by fermentation processes. Modulation of the expression of the MP nucleic acids of the invention, or modification of the sequence of the MP nucleic acid molecules of the
20 invention, can be used to modulate the production of one or more fine chemicals from a microorganism (*e.g.*, to improve the yield or production of one or more fine chemicals from a *Corynebacterium* or *Brevibacterium* species).

The MP nucleic acids of the invention may also be used to identify an organism as being *Corynebacterium glutamicum* or a close relative thereof, or to identify the
25 presence of *C. glutamicum* or a relative thereof in a mixed population of microorganisms. The invention provides the nucleic acid sequences of a number of *C. glutamicum* genes; by probing the extracted genomic DNA of a culture of a unique or mixed population of microorganisms under stringent conditions with a probe spanning a region of a *C. glutamicum* gene which is unique to this organism, one can ascertain
30 whether this organism is present. Although *Corynebacterium glutamicum* itself is nonpathogenic, it is related to species pathogenic in humans, such as *Corynebacterium*

diphtheriae (the causative agent of diphtheria); the detection of such organisms is of significant clinical relevance.

The MP nucleic acid molecules of the invention may also serve as reference points for mapping of the *C. glutamicum* genome, or of genomes of related organisms.

- 5 Similarly, these molecules, or variants or portions thereof, may serve as markers for genetically engineered *Corynebacterium* or *Brevibacterium* species.

- The MP proteins encoded by the novel nucleic acid molecules of the invention are capable of, for example, performing an enzymatic step involved in the metabolism of certain fine chemicals, including amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, and trehalose. Given the availability of cloning vectors for use in *Corynebacterium glutamicum*, such as those disclosed in Sinskey *et al.*, U.S. Patent No. 4,649,119, and techniques for genetic manipulation of *C. glutamicum* and the related *Brevibacterium* species (*e.g.*, *lactofermentum*) (Yoshihama *et al.*, *J. Bacteriol.* 162: 591-597 (1985); Katsumata *et al.*, *J. Bacteriol.* 159: 306-311 (1984); and
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15 Santamaria *et al.*, *J. Gen. Microbiol.* 130: 2237-2246 (1984)), the nucleic acid molecules of the invention may be utilized in the genetic engineering of this organism to make it a better or more efficient producer of one or more fine chemicals.

- This improved production or efficiency of production of a fine chemical may be due to a direct effect of manipulation of a gene of the invention, or it may be due to an
- 20 indirect effect of such manipulation. Specifically, alterations in *C. glutamicum* metabolic pathways for amino acids, vitamins, cofactors, nucleotides, and trehalose may have a direct impact on the overall production of one or more of these desired compounds from this organism. For example, optimizing the activity of a lysine biosynthetic pathway protein or decreasing the activity of a lysine degradative pathway
- 25 protein may result in an increase in the yield or efficiency of production of lysine from such an engineered organism. Alterations in the proteins involved in these metabolic pathways may also have an indirect impact on the production or efficiency of production of a desired fine chemical. For example, a reaction which is in competition for an intermediate necessary for the production of a desired molecule may be eliminated, or a
- 30 pathway necessary for the production of a particular intermediate for a desired compound may be optimized. Further, modulations in the biosynthesis or degradation of, for example, an amino acid, a vitamin, or a nucleotide may increase the overall

ability of the microorganism to rapidly grow and divide, thus increasing the number and/or production capacities of the microorganism in culture and thereby increasing the possible yield of the desired fine chemical.

The nucleic acid and protein molecules of the invention may be utilized to
5 directly improve the production or efficiency of production of one or more desired fine chemicals from *Corynebacterium glutamicum*. Using recombinant genetic techniques well known in the art, one or more of the biosynthetic or degradative enzymes of the invention for amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, or trehalose may be manipulated such that its function is modulated. For example, a
10 biosynthetic enzyme may be improved in efficiency, or its allosteric control region destroyed such that feedback inhibition of production of the compound is prevented. Similarly, a degradative enzyme may be deleted or modified by substitution, deletion, or addition such that its degradative activity is lessened for the desired compound without impairing the viability of the cell. In each case, the overall yield or rate of production of
15 the desired fine chemical may be increased.

It is also possible that such alterations in the protein and nucleotide molecules of the invention may improve the production of other fine chemicals besides the amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, and trehalose through indirect mechanisms. Metabolism of any one compound is necessarily
20 intertwined with other biosynthetic and degradative pathways within the cell, and necessary cofactors, intermediates, or substrates in one pathway are likely supplied or limited by another such pathway. Therefore, by modulating the activity of one or more of the proteins of the invention, the production or efficiency of activity of another fine chemical biosynthetic or degradative pathway may be impacted. For example, amino
25 acids serve as the structural units of all proteins, yet may be present intracellularly in levels which are limiting for protein synthesis; therefore, by increasing the efficiency of production or the yields of one or more amino acids within the cell, proteins, such as biosynthetic or degradative proteins, may be more readily synthesized. Likewise, an alteration in a metabolic pathway enzyme such that a particular side reaction becomes
30 more or less favored may result in the over- or under-production of one or more compounds which are utilized as intermediates or substrates for the production of a desired fine chemical.

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This invention provides novel nucleic acid molecules which encode proteins, referred to herein as metabolic pathway proteins (MP), which are capable of, for example, performing an enzymatic step involved in the metabolism of molecules important for the normal functioning of cells, such as amino acids, vitamins, cofactors, nucleotides and nucleosides, or trehalose. Nucleic acid molecules encoding an MP protein are referred to herein as MP nucleic acid molecules. In a preferred embodiment, the MP protein performs an enzymatic step related to the metabolism of one or more of the following: amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, and trehalose. Examples of such proteins include those encoded by the genes set forth in Table 1.

Accordingly, one aspect of the invention pertains to isolated nucleic acid molecules (*e.g.*, cDNAs, DNAs, or RNAs) comprising a nucleotide sequence encoding an MP protein or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection or amplification of MP-encoding nucleic acid (*e.g.*, DNA or mRNA). In particularly preferred embodiments, the isolated nucleic acid molecule comprises one of the nucleotide sequences set forth as the odd-numbered SEQ ID NOs in the Sequence Listing (*e.g.*, SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7....), or the coding region or a complement thereof of one of these nucleotide sequences. In other particularly preferred embodiments, the isolated nucleic acid molecule of the invention comprises a nucleotide sequence which hybridizes to or is at least about 50%, preferably at least about 60%, more preferably at least about 70%, 80% or 90%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to a nucleotide sequence set forth as an odd-numbered SEQ ID NO in the Sequence Listing (*e.g.*, SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7....), or a portion thereof. In other preferred embodiments, the isolated nucleic acid molecule encodes one of the amino acid sequences set forth as an even-numbered SEQ ID NO in the Sequence Listing (*e.g.*, SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8....). The preferred MP proteins of the present invention also preferably possess at least one of the MP activities described herein.

In another embodiment, the isolated nucleic acid molecule encodes a protein or portion thereof wherein the protein or portion thereof includes an amino acid sequence which is sufficiently homologous to an amino acid sequence of the invention (*e.g.*, a

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sequence having an even-numbered SEQ ID NO: in the Sequence Listing), *e.g.*, sufficiently homologous to an amino acid sequence of the invention such that the protein or portion thereof maintains an MP activity. Preferably, the protein or portion thereof encoded by the nucleic acid molecule maintains the ability to perform an enzymatic

5 reaction in a amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway. In one embodiment, the protein encoded by the nucleic acid molecule is at least about 50%, preferably at least about 60%, and more preferably at least about 70%, 80%, or 90% and most preferably at least about 95%, 96%, 97%, 98%, or 99% or more homologous to an amino acid sequence of the invention (*e.g.*, an

10 entire amino acid sequence selected from those having an even-numbered SEQ ID NO in the Sequence Listing). In another preferred embodiment, the protein is a full length *C. glutamicum* protein which is substantially homologous to an entire amino acid sequence of the invention (encoded by an open reading frame shown in the corresponding odd-numbered SEQ ID NOs in the Sequence Listing (*e.g.*, SEQ ID NO:1,

15 SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7....)).

In another preferred embodiment, the isolated nucleic acid molecule is derived from *C. glutamicum* and encodes a protein (*e.g.*, an MP fusion protein) which includes a biologically active domain which is at least about 50% or more homologous to one of the amino acid sequences of the invention (*e.g.*, a sequence of one of the even-numbered

20 SEQ ID NOs in the Sequence Listing) and is able to catalyze a reaction in a metabolic pathway for an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose, or one or more of the activities set forth in Table 1, and which also includes heterologous nucleic acid sequences encoding a heterologous polypeptide or regulatory regions.

25 In another embodiment, the isolated nucleic acid molecule is at least 15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising a nucleotide sequence of the invention (*e.g.*, a sequence of an odd-numbered SEQ ID NO in the Sequence Listing). Preferably, the isolated nucleic acid molecule corresponds to a naturally-occurring nucleic acid molecule. More preferably,

30 the isolated nucleic acid encodes a naturally-occurring *C. glutamicum* MP protein, or a biologically active portion thereof.

Another aspect of the invention pertains to vectors, *e.g.*, recombinant expression vectors, containing the nucleic acid molecules of the invention, and host cells into which such vectors have been introduced. In one embodiment, such a host cell is used to produce an MP protein by culturing the host cell in a suitable medium. The MP protein
5 can be then isolated from the medium or the host cell.

Yet another aspect of the invention pertains to a genetically altered microorganism in which an MP gene has been introduced or altered. In one embodiment, the genome of the microorganism has been altered by introduction of a nucleic acid molecule of the invention encoding wild-type or mutated MP sequence as a
10 transgene. In another embodiment, an endogenous MP gene within the genome of the microorganism has been altered, *e.g.*, functionally disrupted, by homologous recombination with an altered MP gene. In another embodiment, an endogenous or introduced MP gene in a microorganism has been altered by one or more point mutations, deletions, or inversions, but still encodes a functional MP protein. In still
15 another embodiment, one or more of the regulatory regions (*e.g.*, a promoter, repressor, or inducer) of an MP gene in a microorganism has been altered (*e.g.*, by deletion, truncation, inversion, or point mutation) such that the expression of the MP gene is modulated. In a preferred embodiment, the microorganism belongs to the genus *Corynebacterium* or *Brevibacterium*, with *Corynebacterium glutamicum* being
20 particularly preferred. In a preferred embodiment, the microorganism is also utilized for the production of a desired compound, such as an amino acid, with lysine being particularly preferred.

In another aspect, the invention provides a method of identifying the presence or activity of *Corynebacterium diphtheriae* in a subject. This method includes detection of
25 one or more of the nucleic acid or amino acid sequences of the invention (*e.g.*, the sequences set forth in the Sequence Listing as SEQ ID NOs 1 through 1156) in a subject, thereby detecting the presence or activity of *Corynebacterium diphtheriae* in the subject.

Still another aspect of the invention pertains to an isolated MP protein or a
30 portion, *e.g.*, a biologically active portion, thereof. In a preferred embodiment, the isolated MP protein or portion thereof can catalyze an enzymatic reaction involved in one or more pathways for the metabolism of an amino acid, a vitamin, a cofactor, a

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nutraceutical, a nucleotide, a nucleoside, or trehalose. In another preferred embodiment, the isolated MP protein or portion thereof is sufficiently homologous to an amino acid sequence of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: in the Sequence Listing) such that the protein or portion thereof maintains the ability to

5 catalyze an enzymatic reaction involved in one or more pathways for the metabolism of an amino acid, a vitamin, a cofactor, a nutraceutical, a nucleotide, a nucleoside, or trehalose.

The invention also provides an isolated preparation of an MP protein. In preferred embodiments, the MP protein comprises an amino acid sequence of the

10 invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence Listing). In another preferred embodiment, the invention pertains to an isolated full length protein which is substantially homologous to an entire amino acid sequence of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) (encoded by an open reading frame set forth in a corresponding odd-numbered SEQ ID NO: of the

15 Sequence Listing). In yet another embodiment, the protein is at least about 50%, preferably at least about 60%, and more preferably at least about 70%, 80%, or 90%, and most preferably at least about 95%, 96%, 97%, 98%, or 99% or more homologous to an entire amino acid sequence of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence Listing). In other embodiments, the isolated MP protein

20 comprises an amino acid sequence which is at least about 50% or more homologous to one of the amino acid sequences of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) and is able to catalyze an enzymatic reaction in an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway, or has one or more of the activities set forth in Table 1.

25 Alternatively, the isolated MP protein can comprise an amino acid sequence which is encoded by a nucleotide sequence which hybridizes, *e.g.*, hybridizes under stringent conditions, or is at least about 50%, preferably at least about 60%, more preferably at least about 70%, 80%, or 90%, and even more preferably at least about 95%, 96%, 97%, 98%, or 99% or more homologous to a nucleotide sequence of one of

30 the even-numbered SEQ ID NOs set forth in the Sequence Listing. It is also preferred that the preferred forms of MP proteins also have one or more of the MP bioactivities described herein.

The MP polypeptide, or a biologically active portion thereof, can be operatively linked to a non-MP polypeptide to form a fusion protein. In preferred embodiments, this fusion protein has an activity which differs from that of the MP protein alone. In other preferred embodiments, this fusion protein, when introduced into a *C. glutamicum* pathway for the metabolism of an amino acid, vitamin, cofactor, nutraceutical, results in increased yields and/or efficiency of production of a desired fine chemical from *C. glutamicum*. In particularly preferred embodiments, integration of this fusion protein into an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway of a host cell modulates production of a desired compound from the cell.

In another aspect, the invention provides methods for screening molecules which modulate the activity of an MP protein, either by interacting with the protein itself or a substrate or binding partner of the MP protein, or by modulating the transcription or translation of an MP nucleic acid molecule of the invention.

Another aspect of the invention pertains to a method for producing a fine chemical. This method involves the culturing of a cell containing a vector directing the expression of an MP nucleic acid molecule of the invention, such that a fine chemical is produced. In a preferred embodiment, this method further includes the step of obtaining a cell containing such a vector, in which a cell is transfected with a vector directing the expression of an MP nucleic acid. In another preferred embodiment, this method further includes the step of recovering the fine chemical from the culture. In a particularly preferred embodiment, the cell is from the genus *Corynebacterium* or *Brevibacterium*, or is selected from those strains set forth in Table 3.

Another aspect of the invention pertains to methods for modulating production of a molecule from a microorganism. Such methods include contacting the cell with an agent which modulates MP protein activity or MP nucleic acid expression such that a cell associated activity is altered relative to this same activity in the absence of the agent. In a preferred embodiment, the cell is modulated for one or more *C. glutamicum* amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathways, such that the yields or rate of production of a desired fine chemical by this microorganism is improved. The agent which modulates MP protein activity can be an agent which stimulates MP protein activity or MP nucleic acid expression.

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Examples of agents which stimulate MP protein activity or MP nucleic acid expression include small molecules, active MP proteins, and nucleic acids encoding MP proteins that have been introduced into the cell. Examples of agents which inhibit MP activity or expression include small molecules, and antisense MP nucleic acid molecules.

- 5 Another aspect of the invention pertains to methods for modulating yields of a desired compound from a cell, involving the introduction of a wild-type or mutant MP gene into a cell, either maintained on a separate plasmid or integrated into the genome of the host cell. If integrated into the genome, such integration can be random, or it can take place by homologous recombination such that the native gene is replaced by the
- 10 introduced copy, causing the production of the desired compound from the cell to be modulated. In a preferred embodiment, said yields are increased. In another preferred embodiment, said chemical is a fine chemical. In a particularly preferred embodiment, said fine chemical is an amino acid. In especially preferred embodiments, said amino acid is L-lysine.

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Detailed Description of the Invention

- The present invention provides MP nucleic acid and protein molecules which are involved in the metabolism of certain fine chemicals in *Corynebacterium glutamicum*, including amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, and
- 20 trehalose. The molecules of the invention may be utilized in the modulation of production of fine chemicals from microorganisms, such as *C. glutamicum*, either directly (*e.g.*, where modulation of the activity of a lysine biosynthesis protein has a direct impact on the production or efficiency of production of lysine from that organism), or may have an indirect impact which nonetheless results in an increase of
- 25 yield or efficiency of production of the desired compound (*e.g.*, where modulation of the activity of a nucleotide biosynthesis protein has an impact on the production of an organic acid or a fatty acid from the bacterium, perhaps due to improved growth or an increased supply of necessary co-factors, energy compounds, or precursor molecules). Aspects of the invention are further explicated below.

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I. Fine Chemicals

The term 'fine chemical' is art-recognized and includes molecules produced by an organism which have applications in various industries, such as, but not limited to, the pharmaceutical, agriculture, and cosmetics industries. Such compounds include

5 organic acids, such as tartaric acid, itaconic acid, and diaminopimelic acid, both proteinogenic and non-proteinogenic amino acids, purine and pyrimidine bases, nucleosides, and nucleotides (as described *e.g.* in Kuninaka, A. (1996) Nucleotides and related compounds, p. 561-612, in Biotechnology vol. 6, Rehm *et al.*, eds. VCH: Weinheim, and references contained therein), lipids, both saturated and unsaturated fatty

10 acids (*e.g.*, arachidonic acid), diols (*e.g.*, propane diol, and butane diol), carbohydrates (*e.g.*, hyaluronic acid and trehalose), aromatic compounds (*e.g.*, aromatic amines, vanillin, and indigo), vitamins and cofactors (as described in Ullmann's Encyclopedia of Industrial Chemistry, vol. A27, "Vitamins", p. 443-613 (1996) VCH: Weinheim and references therein; and Ong, A.S., Niki, E. & Packer, L. (1995) "Nutrition, Lipids,

15 Health, and Disease" Proceedings of the UNESCO/Confederation of Scientific and Technological Associations in Malaysia, and the Society for Free Radical Research – Asia, held Sept. 1-3, 1994 at Penang, Malaysia, AOCS Press, (1995)), enzymes, polyketides (Cane *et al.* (1998) *Science* 282: 63-68), and all other chemicals described in Gutcho (1983) Chemicals by Fermentation, Noyes Data Corporation, ISBN:

20 0818805086 and references therein. The metabolism and uses of certain of these fine chemicals are further explicated below.

A. Amino Acid Metabolism and Uses

Amino acids comprise the basic structural units of all proteins, and as such are

25 essential for normal cellular functioning in all organisms. The term "amino acid" is art-recognized. The proteinogenic amino acids, of which there are 20 species, serve as structural units for proteins, in which they are linked by peptide bonds, while the nonproteinogenic amino acids (hundreds of which are known) are not normally found in proteins (see Ullmann's Encyclopedia of Industrial Chemistry, vol. A2, p. 57-97 VCH:

30 Weinheim (1985)). Amino acids may be in the D- or L- optical configuration, though L-amino acids are generally the only type found in naturally-occurring proteins. Biosynthetic and degradative pathways of each of the 20 proteinogenic amino acids

have been well characterized in both prokaryotic and eukaryotic cells (see, for example, Stryer, L. *Biochemistry*, 3rd edition, pages 578-590 (1988)). The 'essential' amino acids (histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine), so named because they are generally a nutritional requirement due to the complexity of their biosyntheses, are readily converted by simple biosynthetic pathways to the remaining 11 'nonessential' amino acids (alanine, arginine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, and tyrosine). Higher animals do retain the ability to synthesize some of these amino acids, but the essential amino acids must be supplied from the diet in order for normal protein synthesis to occur.

Aside from their function in protein biosynthesis, these amino acids are interesting chemicals in their own right, and many have been found to have various applications in the food, feed, chemical, cosmetics, agriculture, and pharmaceutical industries. Lysine is an important amino acid in the nutrition not only of humans, but also of monogastric animals such as poultry and swine. Glutamate is most commonly used as a flavor additive (mono-sodium glutamate, MSG) and is widely used throughout the food industry, as are aspartate, phenylalanine, glycine, and cysteine. Glycine, L-methionine and tryptophan are all utilized in the pharmaceutical industry. Glutamine, valine, leucine, isoleucine, histidine, arginine, proline, serine and alanine are of use in both the pharmaceutical and cosmetics industries. Threonine, tryptophan, and D/ L-methionine are common feed additives. (Leuchtenberger, W. (1996) *Amino acids - technical production and use*, p. 466-502 in Rehm *et al.* (eds.) *Biotechnology* vol. 6, chapter 14a, VCH: Weinheim). Additionally, these amino acids have been found to be useful as precursors for the synthesis of synthetic amino acids and proteins, such as N-acetylcysteine, S-carboxymethyl-L-cysteine, (S)-5-hydroxytryptophan, and others described in Ulmann's *Encyclopedia of Industrial Chemistry*, vol. A2, p. 57-97, VCH: Weinheim, 1985.

The biosynthesis of these natural amino acids in organisms capable of producing them, such as bacteria, has been well characterized (for review of bacterial amino acid biosynthesis and regulation thereof, see Umbarger, H.E. (1978) *Ann. Rev. Biochem.* 47: 533-606). Glutamate is synthesized by the reductive amination of α -ketoglutarate, an intermediate in the citric acid cycle. Glutamine, proline, and arginine are each subsequently produced from glutamate. The biosynthesis of serine is a three-

step process beginning with 3-phosphoglycerate (an intermediate in glycolysis), and resulting in this amino acid after oxidation, transamination, and hydrolysis steps. Both cysteine and glycine are produced from serine; the former by the condensation of homocysteine with serine, and the latter by the transferal of the side-chain β -carbon atom to tetrahydrofolate, in a reaction catalyzed by serine transhydroxymethylase. Phenylalanine, and tyrosine are synthesized from the glycolytic and pentose phosphate pathway precursors erythrose 4-phosphate and phosphoenolpyruvate in a 9-step biosynthetic pathway that differ only at the final two steps after synthesis of prephenate. Tryptophan is also produced from these two initial molecules, but its synthesis is an 11-step pathway. Tyrosine may also be synthesized from phenylalanine, in a reaction catalyzed by phenylalanine hydroxylase. Alanine, valine, and leucine are all biosynthetic products of pyruvate, the final product of glycolysis. Aspartate is formed from oxaloacetate, an intermediate of the citric acid cycle. Asparagine, methionine, threonine, and lysine are each produced by the conversion of aspartate. Isoleucine is formed from threonine. A complex 9-step pathway results in the production of histidine from 5-phosphoribosyl-1-pyrophosphate, an activated sugar.

Amino acids in excess of the protein synthesis needs of the cell cannot be stored, and are instead degraded to provide intermediates for the major metabolic pathways of the cell (for review see Stryer, L. Biochemistry 3rd ed. Ch. 21 "Amino Acid Degradation and the Urea Cycle" p. 495-516 (1988)). Although the cell is able to convert unwanted amino acids into useful metabolic intermediates, amino acid production is costly in terms of energy, precursor molecules, and the enzymes necessary to synthesize them. Thus it is not surprising that amino acid biosynthesis is regulated by feedback inhibition, in which the presence of a particular amino acid serves to slow or entirely stop its own production (for overview of feedback mechanisms in amino acid biosynthetic pathways, see Stryer, L. Biochemistry, 3rd ed. Ch. 24: "Biosynthesis of Amino Acids and Heme" p. 575-600 (1988)). Thus, the output of any particular amino acid is limited by the amount of that amino acid present in the cell.

B. Vitamin, Cofactor, and Nutraceutical Metabolism and Uses

Vitamins, cofactors, and nutraceuticals comprise another group of molecules which the higher animals have lost the ability to synthesize and so must ingest, although

they are readily synthesized by other organisms, such as bacteria. These molecules are either bioactive substances themselves, or are precursors of biologically active substances which may serve as electron carriers or intermediates in a variety of metabolic pathways. Aside from their nutritive value, these compounds also have

5 significant industrial value as coloring agents, antioxidants, and catalysts or other processing aids. (For an overview of the structure, activity, and industrial applications of these compounds, see, for example, Ullman's Encyclopedia of Industrial Chemistry, "Vitamins" vol. A27, p. 443-613, VCH: Weinheim, 1996.) The term "vitamin" is art-

10 recognized, and includes nutrients which are required by an organism for normal functioning, but which that organism cannot synthesize by itself. The group of vitamins may encompass cofactors and nutraceutical compounds. The language "cofactor" includes nonproteinaceous compounds required for a normal enzymatic activity to occur. Such compounds may be organic or inorganic; the cofactor molecules of the

15 invention are preferably organic. The term "nutraceutical" includes dietary supplements having health benefits in plants and animals, particularly humans. Examples of such molecules are vitamins, antioxidants, and also certain lipids (*e.g.*, polyunsaturated fatty acids).

The biosynthesis of these molecules in organisms capable of producing them, such as bacteria, has been largely characterized (Ullman's Encyclopedia of Industrial

20 Chemistry, "Vitamins" vol. A27, p. 443-613, VCH: Weinheim, 1996; Michal, G. (1999) Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, John Wiley & Sons; Ong, A.S., Niki, E. & Packer, L. (1995) "Nutrition, Lipids, Health, and Disease" Proceedings of the UNESCO/Confederation of Scientific and Technological Associations in Malaysia, and the Society for Free Radical Research – Asia, held Sept.

25 1-3, 1994 at Penang, Malaysia, AOCS Press: Champaign, IL X, 374 S).

Thiamin (vitamin B₁) is produced by the chemical coupling of pyrimidine and thiazole moieties. Riboflavin (vitamin B₂) is synthesized from guanosine-5'-triphosphate (GTP) and ribose-5'-phosphate. Riboflavin, in turn, is utilized for the synthesis of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD). The family of

30 compounds collectively termed 'vitamin B₆' (*e.g.*, pyridoxine, pyridoxamine, pyridoxa-5'-phosphate, and the commercially used pyridoxin hydrochloride) are all derivatives of the common structural unit, 5-hydroxy-6-methylpyridine. Pantothenate (pantothenic

acid, (R)-(+)-N-(2,4-dihydroxy-3,3-dimethyl-1-oxobutyl)- β -alanine) can be produced either by chemical synthesis or by fermentation. The final steps in pantothenate biosynthesis consist of the ATP-driven condensation of β -alanine and pantoic acid. The enzymes responsible for the biosynthesis steps for the conversion to pantoic acid, to β -alanine and for the condensation to panthothenic acid are known. The metabolically active form of pantothenate is Coenzyme A, for which the biosynthesis proceeds in 5 enzymatic steps. Pantothenate, pyridoxal-5'-phosphate, cysteine and ATP are the precursors of Coenzyme A. These enzymes not only catalyze the formation of panthothante, but also the production of (R)-pantoic acid, (R)-pantolacton, (R)-panthenol (provitamin B₅), pantetheine (and its derivatives) and coenzyme A.

Biotin biosynthesis from the precursor molecule pimeloyl-CoA in microorganisms has been studied in detail and several of the genes involved have been identified. Many of the corresponding proteins have been found to also be involved in Fe-cluster synthesis and are members of the nifS class of proteins. Lipic acid is derived from octanoic acid, and serves as a coenzyme in energy metabolism, where it becomes part of the pyruvate dehydrogenase complex and the α -ketoglutarate dehydrogenase complex. The folates are a group of substances which are all derivatives of folic acid, which is turn is derived from L-glutamic acid, p-amino-benzoic acid and 6-methylpterin. The biosynthesis of folic acid and its derivatives, starting from the metabolism intermediates guanosine-5'-triphosphate (GTP), L-glutamic acid and p-amino-benzoic acid has been studied in detail in certain microorganisms.

Corrinoids (such as the cobalamines and particularly vitamin B₁₂) and porphyrines belong to a group of chemicals characterized by a tetrapyrrole ring system. The biosynthesis of vitamin B₁₂ is sufficiently complex that it has not yet been completely characterized, but many of the enzymes and substrates involved are now known. Nicotinic acid (nicotinate), and nicotinamide are pyridine derivatives which are also termed 'niacin'. Niacin is the precursor of the important coenzymes NAD (nicotinamide adenine dinucleotide) and NADP (nicotinamide adenine dinucleotide phosphate) and their reduced forms.

The large-scale production of these compounds has largely relied on cell-free chemical syntheses, though some of these chemicals have also been produced by large-scale culture of microorganisms, such as riboflavin, Vitamin B₆, pantothenate, and

biotin. Only Vitamin B₁₂ is produced solely by fermentation, due to the complexity of its synthesis. *In vitro* methodologies require significant inputs of materials and time, often at great cost.

5 C. Purine, Pyrimidine, Nucleoside and Nucleotide Metabolism and Uses

Purine and pyrimidine metabolism genes and their corresponding proteins are important targets for the therapy of tumor diseases and viral infections. The language "purine" or "pyrimidine" includes the nitrogenous bases which are constituents of nucleic acids, co-enzymes, and nucleotides. The term "nucleotide" includes the basic
10 structural units of nucleic acid molecules, which are comprised of a nitrogenous base, a pentose sugar (in the case of RNA, the sugar is ribose; in the case of DNA, the sugar is D-deoxyribose), and phosphoric acid. The language "nucleoside" includes molecules which serve as precursors to nucleotides, but which are lacking the phosphoric acid moiety that nucleotides possess. By inhibiting the biosynthesis of these molecules, or
15 their mobilization to form nucleic acid molecules, it is possible to inhibit RNA and DNA synthesis; by inhibiting this activity in a fashion targeted to cancerous cells, the ability of tumor cells to divide and replicate may be inhibited. Additionally, there are nucleotides which do not form nucleic acid molecules, but rather serve as energy stores (*i.e.*, AMP) or as coenzymes (*i.e.*, FAD and NAD).

20 Several publications have described the use of these chemicals for these medical indications, by influencing purine and/or pyrimidine metabolism (*e.g.* Christopherson, R.I. and Lyons, S.D. (1990) "Potent inhibitors of *de novo* pyrimidine and purine biosynthesis as chemotherapeutic agents." *Med. Res. Reviews* 10: 505-548). Studies of enzymes involved in purine and pyrimidine metabolism have been focused on the
25 development of new drugs which can be used, for example, as immunosuppressants or anti-proliferants (Smith, J.L., (1995) "Enzymes in nucleotide synthesis." *Curr. Opin. Struct. Biol.* 5: 752-757; (1995) *Biochem Soc. Transact.* 23: 877-902). However, purine and pyrimidine bases, nucleosides and nucleotides have other utilities: as intermediates in the biosynthesis of several fine chemicals (*e.g.*, thiamine, S-adenosyl-methionine,
30 folates, or riboflavin), as energy carriers for the cell (*e.g.*, ATP or GTP), and for chemicals themselves, commonly used as flavor enhancers (*e.g.*, IMP or GMP) or for several medicinal applications (see, for example, Kuninaka, A. (1996) Nucleotides and

Related Compounds in Biotechnology vol. 6, Rehm *et al.*, eds. VCH: Weinheim, p. 561-612). Also, enzymes involved in purine, pyrimidine, nucleoside, or nucleotide metabolism are increasingly serving as targets against which chemicals for crop protection, including fungicides, herbicides and insecticides, are developed.

- 5 The metabolism of these compounds in bacteria has been characterized (for reviews see, for example, Zalkin, H. and Dixon, J.E. (1992) "*de novo* purine nucleotide biosynthesis", in: Progress in Nucleic Acid Research and Molecular Biology, vol. 42, Academic Press:, p. 259-287; and Michal, G. (1999) "Nucleotides and Nucleosides", Chapter 8 in: Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology,
- 10 Wiley: New York). Purine metabolism has been the subject of intensive research, and is essential to the normal functioning of the cell. Impaired purine metabolism in higher animals can cause severe disease, such as gout. Purine nucleotides are synthesized from ribose-5-phosphate, in a series of steps through the intermediate compound inosine-5'-phosphate (IMP), resulting in the production of guanosine-5'-monophosphate (GMP) or
- 15 adenosine-5'-monophosphate (AMP), from which the triphosphate forms utilized as nucleotides are readily formed. These compounds are also utilized as energy stores, so their degradation provides energy for many different biochemical processes in the cell. Pyrimidine biosynthesis proceeds by the formation of uridine-5'-monophosphate (UMP) from ribose-5-phosphate. UMP, in turn, is converted to cytidine-5'-triphosphate (CTP).
- 20 The deoxy- forms of all of these nucleotides are produced in a one step reduction reaction from the diphosphate ribose form of the nucleotide to the diphosphate deoxyribose form of the nucleotide. Upon phosphorylation, these molecules are able to participate in DNA synthesis.

25 *D. Trehalose Metabolism and Uses*

- Trehalose consists of two glucose molecules, bound in α , α -1,1 linkage. It is commonly used in the food industry as a sweetener, an additive for dried or frozen foods, and in beverages. However, it also has applications in the pharmaceutical, cosmetics and biotechnology industries (see, for example, Nishimoto *et al.*, (1998) U.S.
- 30 Patent No. 5,759,610; Singer, M.A. and Lindquist, S. (1998) *Trends Biotech.* 16: 460-467; Paiva, C.L.A. and Panek, A.D. (1996) *Biotech. Ann. Rev.* 2: 293-314; and Shiosaka, M. (1997) *J. Japan* 172: 97-102). Trehalose is produced by enzymes from

many microorganisms and is naturally released into the surrounding medium, from which it can be collected using methods known in the art.

II. Elements and Methods of the Invention

5 The present invention is based, at least in part, on the discovery of novel molecules, referred to herein as MP nucleic acid and protein molecules, which play a role in or function in one or more cellular metabolic pathways. In one embodiment, the MP molecules catalyze an enzymatic reaction involving one or more amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic
10 pathways. In a preferred embodiment, the activity of the MP molecules of the present invention in one or more *C. glutamicum* metabolic pathways for amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides or trehalose has an impact on the production of a desired fine chemical by this organism. In a particularly preferred embodiment, the MP molecules of the invention are modulated in activity, such that the
15 *C. glutamicum* metabolic pathways in which the MP proteins of the invention are involved are modulated in efficiency or output, which either directly or indirectly modulates the production or efficiency of production of a desired fine chemical by *C. glutamicum*.

 The language, "MP protein" or "MP polypeptide" includes proteins which play
20 a role in, *e.g.*, catalyze an enzymatic reaction, in one or more amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside or trehalose metabolic pathways. Examples of MP proteins include those encoded by the MP genes set forth in Table 1 and by the odd-numbered SEQ ID NOs. The terms "MP gene" or "MP nucleic acid sequence" include nucleic acid sequences encoding an MP protein, which consist of a
25 coding region and also corresponding untranslated 5' and 3' sequence regions. Examples of MP genes include those set forth in Table 1. The terms "production" or "productivity" are art-recognized and include the concentration of the fermentation product (for example, the desired fine chemical) formed within a given time and a given fermentation volume (*e.g.*, kg product per hour per liter). The term "efficiency of
30 production" includes the time required for a particular level of production to be achieved (for example, how long it takes for the cell to attain a particular rate of output of a fine chemical). The term "yield" or "product/carbon yield" is art-recognized and includes

the efficiency of the conversion of the carbon source into the product (*i.e.*, fine chemical). This is generally written as, for example, kg product per kg carbon source. By increasing the yield or production of the compound, the quantity of recovered molecules, or of useful recovered molecules of that compound in a given amount of culture over a given amount of time is increased. The terms "biosynthesis" or a "biosynthetic pathway" are art-recognized and include the synthesis of a compound, preferably an organic compound, by a cell from intermediate compounds in what may be a multistep and highly regulated process. The terms "degradation" or a "degradation pathway" are art-recognized and include the breakdown of a compound, preferably an organic compound, by a cell to degradation products (generally speaking, smaller or less complex molecules) in what may be a multistep and highly regulated process. The language "metabolism" is art-recognized and includes the totality of the biochemical reactions that take place in an organism. The metabolism of a particular compound, then, (*e.g.*, the metabolism of an amino acid such as glycine) comprises the overall biosynthetic, modification, and degradation pathways in the cell related to this compound.

In another embodiment, the MP molecules of the invention are capable of modulating the production of a desired molecule, such as a fine chemical, in a microorganism such as *C. glutamicum*. Using recombinant genetic techniques, one or more of the biosynthetic or degradative enzymes of the invention for amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, or trehalose may be manipulated such that its function is modulated. For example, a biosynthetic enzyme may be improved in efficiency, or its allosteric control region destroyed such that feedback inhibition of production of the compound is prevented. Similarly, a degradative enzyme may be deleted or modified by substitution, deletion, or addition such that its degradative activity is lessened for the desired compound without impairing the viability of the cell. In each case, the overall yield or rate of production of one of these desired fine chemicals may be increased.

It is also possible that such alterations in the protein and nucleotide molecules of the invention may improve the production of other fine chemicals besides the amino acids, vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, and trehalose. Metabolism of any one compound is necessarily intertwined with other biosynthetic and

degradative pathways within the cell, and necessary cofactors, intermediates, or substrates in one pathway are likely supplied or limited by another such pathway. Therefore, by modulating the activity of one or more of the proteins of the invention, the production or efficiency of activity of another fine chemical biosynthetic or degradative pathway may be impacted. For example, amino acids serve as the structural units of all proteins, yet may be present intracellularly in levels which are limiting for protein synthesis; therefore, by increasing the efficiency of production or the yields of one or more amino acids within the cell, proteins, such as biosynthetic or degradative proteins, may be more readily synthesized. Likewise, an alteration in a metabolic pathway enzyme such that a particular side reaction becomes more or less favored may result in the over- or under-production of one or more compounds which are utilized as intermediates or substrates for the production of a desired fine chemical.

The isolated nucleic acid sequences of the invention are contained within the genome of a *Corynebacterium glutamicum* strain available through the American Type Culture Collection, given designation ATCC 13032. The nucleotide sequence of the isolated *C. glutamicum* MP DNAs and the predicted amino acid sequences of the *C. glutamicum* MP proteins are shown in the Sequence Listing as odd-numbered SEQ ID NOs and even-numbered SEQ ID NOs, respectively. Computational analyses were performed which classified and/or identified these nucleotide sequences as sequences which encode metabolic pathway proteins.

The present invention also pertains to proteins which have an amino acid sequence which is substantially homologous to an amino acid sequence of the invention (e.g., the sequence of an even-numbered SEQ ID NO of the Sequence Listing). As used herein, a protein which has an amino acid sequence which is substantially homologous to a selected amino acid sequence is least about 50% homologous to the selected amino acid sequence, e.g., the entire selected amino acid sequence. A protein which has an amino acid sequence which is substantially homologous to a selected amino acid sequence can also be least about 50-60%, preferably at least about 60-70%, and more preferably at least about 70-80%, 80-90%, or 90-95%, and most preferably at least about 96%, 97%, 98%, 99% or more homologous to the selected amino acid sequence.

The MP protein or a biologically active portion or fragment thereof of the invention can catalyze an enzymatic reaction in one or more amino acid, vitamin,

cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathways, or have one or more of the activities set forth in Table 1.

Various aspects of the invention are described in further detail in the following subsections:

5

A. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules that encode MP polypeptides or biologically active portions thereof, as well as nucleic acid fragments sufficient for use as hybridization probes or primers for the identification or
10 amplification of MP-encoding nucleic acid (e.g., MP DNA). As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g., cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. This term also encompasses untranslated sequence located at both the 3' and 5' ends of the coding region of the gene: at least about 100 nucleotides
15 of sequence upstream from the 5' end of the coding region and at least about 20 nucleotides of sequence downstream from the 3' end of the coding region of the gene. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA. An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic
20 acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated MP nucleic acid molecule can contain less than about 5 kb, 4kb, 3kb, 2kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank
25 the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived (e.g., a *C. glutamicum* cell). Moreover, an "isolated" nucleic acid molecule, such as a DNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or chemical precursors or other chemicals when chemically synthesized.

30 A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having a nucleotide sequence of an odd-numbered SEQ ID NO of the Sequence Listing, or a portion thereof, can be isolated using standard molecular biology techniques and the

sequence information provided herein. For example, a *C. glutamicum* MP DNA can be isolated from a *C. glutamicum* library using all or portion of one of the odd-numbered SEQ ID NO sequences of the Sequence Listing as a hybridization probe and standard hybridization techniques (*e.g.*, as described in Sambrook, J., Fritsh, E. F., and Maniatis, 5 T. *Molecular Cloning: A Laboratory Manual*. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989). Moreover, a nucleic acid molecule encompassing all or a portion of one of the nucleic acid sequences of the invention (*e.g.*, an odd-numbered SEQ ID NO:) can be isolated by the polymerase chain reaction using oligonucleotide primers designed based upon this 10 sequence (*e.g.*, a nucleic acid molecule encompassing all or a portion of one of the nucleic acid sequences of the invention (*e.g.*, an odd-numbered SEQ ID NO of the Sequence Listing) can be isolated by the polymerase chain reaction using oligonucleotide primers designed based upon this same sequence). For example, mRNA can be isolated from normal endothelial cells (*e.g.*, by the guanidinium-thiocyanate 15 extraction procedure of Chirgwin *et al.* (1979) *Biochemistry* 18: 5294-5299) and DNA can be prepared using reverse transcriptase (*e.g.*, Moloney MLV reverse transcriptase, available from Gibco/BRL, Bethesda, MD; or AMV reverse transcriptase, available from Scikagaku America, Inc., St. Petersburg, FL). Synthetic oligonucleotide primers for polymerase chain reaction amplification can be designed based upon one of the 20 nucleotide sequences shown in the Sequence Listing. A nucleic acid of the invention can be amplified using cDNA or, alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding 25 to an MP nucleotide sequence can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

In a preferred embodiment, an isolated nucleic acid molecule of the invention comprises one of the nucleotide sequences shown in the Sequence Listing. The nucleic acid sequences of the invention, as set forth in the Sequence Listing, correspond to the 30 *Corynebacterium glutamicum* MP DNAs of the invention. This DNA comprises sequences encoding MP proteins (*i.e.*, the "coding region", indicated in each odd-numbered SEQ ID NO: sequence in the Sequence Listing), as well as 5' untranslated

sequences and 3' untranslated sequences, also indicated in each odd-numbered SEQ ID NO: in the Sequence Listing. Alternatively, the nucleic acid molecule can comprise only the coding region of any of the nucleic acid sequences of the Sequence Listing.

For the purposes of this application, it will be understood that each of the nucleic acid and amino acid sequences set forth in the Sequence Listing has an identifying RXA, RXN, RXS, or RXC number having the designation "RXA", "RXN", "RXS", or "RXC" followed by 5 digits (*i.e.*, RXA00007, RXN00023, RXS00116, or RXC00128). Each of the nucleic acid sequences comprises up to three parts: a 5' upstream region, a coding region, and a downstream region. Each of these three regions is identified by the same RXA, RXN, RXS, or RXC designation to eliminate confusion. The recitation "one of the odd-numbered sequences of the Sequence Listing", then, refers to any of the nucleic acid sequences in the Sequence Listing, which may also be distinguished by their differing RXA, RXN, RXS, or RXC designations. The coding region of each of these sequences is translated into a corresponding amino acid sequence, which is also set forth in the Sequence Listing, as an even-numbered SEQ ID NO: immediately following the corresponding nucleic acid sequence. For example, the coding region for RXA02229 is set forth in SEQ ID NO:1, while the amino acid sequence which it encodes is set forth as SEQ ID NO:2. The sequences of the nucleic acid molecules of the invention are identified by the same RXA, RXN, RXS, or RXC designations as the amino acid molecules which they encode, such that they can be readily correlated. For example, the amino acid sequences designated RXA02229, RX00351, RXS02970, and RXC02390 are translations of the coding regions of the nucleotide sequences of nucleic acid molecules RXA02229, RX00351, RXS02970, and RXC02390, respectively. The correspondence between the RXA, RXN, RXS, and RXC nucleotide and amino acid sequences of the invention and their assigned SEQ ID NOs is set forth in Table 1.

Several of the genes of the invention are "F-designated genes". An F-designated gene includes those genes set forth in Table 1 which have an 'F' in front of the RXA, RXN, RXS, or RXC designation. For example, SEQ ID NO:5, designated, as indicated on Table 1, as "F RXA01009", is an F-designated gene, as are SEQ ID NOs: 73, 75, and 77 (designated on Table 1 as "F RXA00007", "F RXA00364", and "F RXA00367", respectively).

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In one embodiment, the nucleic acid molecules of the present invention are not intended to include *C. glutamicum* those compiled in Table 2. In the case of the dapD gene, a sequence for this gene was published in Wehrmann, A., *et al.* (1998) *J. Bacteriol.* 180(12): 3159-3165. However, the sequence obtained by the inventors of the present application is significantly longer than the published version. It is believed that the published version relied on an incorrect start codon, and thus represents only a fragment of the actual coding region.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of one of the nucleotide sequences of the invention (*e.g.*, a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing), or a portion thereof. A nucleic acid molecule which is complementary to one of the nucleotide sequences of the invention is one which is sufficiently complementary to one of the nucleotide sequences shown in the Sequence Listing (*e.g.*, the sequence of an odd-numbered SEQ ID NO:) such that it can hybridize to one of the nucleotide sequences of the invention, thereby forming a stable duplex.

In still another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleotide sequence which is at least about 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%, more preferably at least about 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to a nucleotide sequence of the invention (*e.g.*, a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing), or a portion thereof. Ranges and identity values intermediate to the above-recited ranges, (*e.g.*, 70-90% identical or 80-95% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper and/or lower limits are intended to be included. In an additional preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleotide sequence which hybridizes, *e.g.*, hybridizes under stringent conditions, to one of the nucleotide sequences of the invention, or a portion thereof.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of the coding region of the sequence of one of the odd-numbered SEQ ID NOs

of the Sequence Listing, for example a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of an MP protein. The nucleotide sequences determined from the cloning of the MP genes from *C. glutamicum* allows for the generation of probes and primers designed for use in identifying and/or cloning MP

5 homologues in other cell types and organisms, as well as MP homologues from other *Corynebacteria* or related species. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 40, 50 or 75 consecutive nucleotides of a sense strand of one

10 of the nucleotide sequences of the invention (*e.g.*, a sequence of one of the odd-numbered SEQ ID NOs of the Sequence Listing), an anti-sense sequence of one of these sequences, or naturally occurring mutants thereof. Primers based on a nucleotide sequence of the invention can be used in PCR reactions to clone MP homologues. Probes based on the MP nucleotide sequences can be used to detect transcripts or

15 genomic sequences encoding the same or homologous proteins. In preferred embodiments, the probe further comprises a label group attached thereto, *e.g.* the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells which misexpress an MP protein, such as by measuring a level of an MP-encoding

20 nucleic acid in a sample of cells from a subject *e.g.*, detecting MP mRNA levels or determining whether a genomic MP gene has been mutated or deleted.

In one embodiment, the nucleic acid molecule of the invention encodes a protein or portion thereof which includes an amino acid sequence which is sufficiently homologous to an amino acid sequence of the invention (*e.g.*, a sequence of an even-

25 numbered SEQ ID NO of the Sequence Listing) such that the protein or portion thereof maintains the ability to catalyze an enzymatic reaction in an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway. As used herein, the language "sufficiently homologous" refers to proteins or portions thereof which have amino acid sequences which include a minimum number of identical or

30 equivalent (*e.g.*, an amino acid residue which has a similar side chain as an amino acid residue in a sequence of one of the even-numbered SEQ ID NOs of the Sequence Listing) amino acid residues to an amino acid sequence of the invention such that the

protein or portion thereof is able to catalyze an enzymatic reaction in a *C. glutamicum* amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside or trehalose metabolic pathway. Protein members of such metabolic pathways, as described herein, function to catalyze the biosynthesis or degradation of one or more of: amino acids,
5 vitamins, cofactors, nutraceuticals, nucleotides, nucleosides, or trehalose. Examples of such activities are also described herein. Thus, "the function of an MP protein" contributes to the overall functioning of one or more such metabolic pathway and contributes, either directly or indirectly, to the yield, production, and/or efficiency of production of one or more fine chemicals. Examples of MP protein activities are set
10 forth in Table 1.

In another embodiment, the protein is at least about 50-60%, preferably at least about 60-70%, and more preferably at least about 70-80%, 80-90%, 90-95%, and most preferably at least about 96%, 97%, 98%, 99% or more homologous to an entire amino acid sequence of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of
15 the Sequence Listing).

Portions of proteins encoded by the MP nucleic acid molecules of the invention are preferably biologically active portions of one of the MP proteins. As used herein, the term "biologically active portion of an MP protein" is intended to include a portion, *e.g.*, a domain/motif, of an MP protein that catalyzes an enzymatic reaction in one or
20 more *C. glutamicum* amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathways, or has an activity as set forth in Table 1. To determine whether an MP protein or a biologically active portion thereof can catalyze an enzymatic reaction in an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway, an assay of enzymatic activity may be performed. Such
25 assay methods are well known to those of ordinary skill in the art, as detailed in Example 8 of the Exemplification.

Additional nucleic acid fragments encoding biologically active portions of an MP protein can be prepared by isolating a portion of one of the amino acid sequences of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence
30 Listing), expressing the encoded portion of the MP protein or peptide (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of the MP protein or peptide.

The invention further encompasses nucleic acid molecules that differ from one of the nucleotide sequences of the invention (*e.g.*, a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing) (and portions thereof) due to degeneracy of the genetic code and thus encode the same MP protein as that encoded by the nucleotide sequences of the invention. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in the Sequence Listing (*e.g.*, an even-numbered SEQ ID NO:). In a still further embodiment, the nucleic acid molecule of the invention encodes a full length *C. glutamicum* protein which is substantially homologous to an amino acid sequence of the invention (encoded by an open reading frame shown in an odd-numbered SEQ ID NO: of the Sequence Listing).

It will be understood by one of ordinary skill in the art that in one embodiment the sequences of the invention are not meant to include the sequences of the prior art, such as those Genbank sequences set forth in Tables 2 or 4 which were available prior to the present invention. In one embodiment, the invention includes nucleotide and amino acid sequences having a percent identity to a nucleotide or amino acid sequence of the invention which is greater than that of a sequence of the prior art (*e.g.*, a Genbank sequence (or the protein encoded by such a sequence) set forth in Tables 2 or 4). For example, the invention includes a nucleotide sequence which is greater than and/or at least 40% identical to the nucleotide sequence designated RXA00115 (SEQ ID NO:185), a nucleotide sequence which is greater than and/or at least % identical to the nucleotide sequence designated RXA00131 (SEQ ID NO:991), and a nucleotide sequence which is greater than and/or at least 39% identical to the nucleotide sequence designated RXA00219 (SEQ ID NO:345). One of ordinary skill in the art would be able to calculate the lower threshold of percent identity for any given sequence of the invention by examining the GAP-calculated percent identity scores set forth in Table 4 for each of the three top hits for the given sequence, and by subtracting the highest GAP-calculated percent identity from 100 percent. One of ordinary skill in the art will also appreciate that nucleic acid and amino acid sequences having percent identities greater than the lower threshold so calculated (*e.g.*, at least 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%, more preferably at least about 71%, 72%, 73%,

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74%, 75%, 76%, 77%, 78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more identical) are also encompassed by the invention.

In addition to the *C. glutamicum* MP nucleotide sequences set forth in the

5 Sequence Listing as odd-numbered SEQ ID NOs, it will be appreciated by one of ordinary skill in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of MP proteins may exist within a population (e.g., the *C. glutamicum* population). Such genetic polymorphism in the MP gene may exist among individuals within a population due to natural variation. As used herein, the terms

10 "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding an MP protein, preferably a *C. glutamicum* MP protein. Such natural variations can typically result in 1-5% variance in the nucleotide sequence of the MP gene. Any and all such nucleotide variations and resulting amino acid

15 functional activity of MP proteins are intended to be within the scope of the invention.

Nucleic acid molecules corresponding to natural variants and non-*C. glutamicum* homologues of the *C. glutamicum* MP DNA of the invention can be isolated based on their homology to the *C. glutamicum* MP nucleic acid disclosed herein using the *C. glutamicum* DNA, or a portion thereof, as a hybridization probe according to standard

20 hybridization techniques under stringent hybridization conditions. Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 15 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising a nucleotide sequence of an odd-numbered SEQ ID NO: of the Sequence Listing. In other embodiments, the nucleic acid is at least 30, 50, 100, 250 or

25 more nucleotides in length. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other. Preferably, the conditions are such that sequences at least about 65%, more preferably at least about 70%, and even more preferably at least about

30 75% or more homologous to each other typically remain hybridized to each other. Such stringent conditions are known to one of ordinary skill in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6.

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A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65°C. Preferably, an isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to a
5 nucleotide sequence of the invention corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (*e.g.*, encodes a natural protein). In one embodiment, the nucleic acid encodes a natural *C. glutamicum* MP protein.

10 In addition to naturally-occurring variants of the MP sequence that may exist in the population, one of ordinary skill in the art will further appreciate that changes can be introduced by mutation into a nucleotide sequence of the invention, thereby leading to changes in the amino acid sequence of the encoded MP protein, without altering the functional ability of the MP protein. For example, nucleotide substitutions leading to
15 amino acid substitutions at "non-essential" amino acid residues can be made in a nucleotide sequence of the invention. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of one of the MP proteins (*e.g.*, an even-numbered SEQ ID NO: of the Sequence Listing) without altering the activity of said MP protein, whereas an "essential" amino acid residue is required for MP protein activity.
20 Other amino acid residues, however, (*e.g.*, those that are not conserved or only semi-conserved in the domain having MP activity) may not be essential for activity and thus are likely to be amenable to alteration without altering MP activity.

Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding MP proteins that contain changes in amino acid residues that are not essential
25 for MP activity. Such MP proteins differ in amino acid sequence from a sequence of an even-numbered SEQ ID NO: of the Sequence Listing yet retain at least one of the MP activities described herein. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 50% homologous to an amino acid sequence of the
30 invention and is capable of catalyzing an enzymatic reaction in an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway, or has one or more activities set forth in Table 1. Preferably, the protein encoded by the nucleic

acid molecule is at least about 50-60% homologous to the amino acid sequence of one of the odd-numbered SEQ ID NOs of the Sequence Listing, more preferably at least about 60-70% homologous to one of these sequences, even more preferably at least about 70-80%, 80-90%, 90-95% homologous to one of these sequences, and most preferably at least about 96%, 97%, 98%, or 99% homologous to one of the amino acid sequences of the invention.

To determine the percent homology of two amino acid sequences (*e.g.*, one of the amino acid sequences of the invention and a mutant form thereof) or of two nucleic acids, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of one protein or nucleic acid for optimal alignment with the other protein or nucleic acid). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in one sequence (*e.g.*, one of the amino acid sequences of the invention) is occupied by the same amino acid residue or nucleotide as the corresponding position in the other sequence (*e.g.*, a mutant form of the amino acid sequence), then the molecules are homologous at that position (*i.e.*, as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity"). The percent homology between the two sequences is a function of the number of identical positions shared by the sequences (*i.e.*, % homology = # of identical positions/total # of positions x 100).

An isolated nucleic acid molecule encoding an MP protein homologous to a protein sequence of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) can be created by introducing one or more nucleotide substitutions, additions or deletions into a nucleotide sequence of the invention such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into one of the nucleotide sequences of the invention by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic

acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in an MP protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an MP coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for an MP activity described herein to identify mutants that retain MP activity. Following mutagenesis of the nucleotide sequence of one of the odd-numbered SEQ ID NOs of the Sequence Listing, the encoded protein can be expressed recombinantly and the activity of the protein can be determined using, for example, assays described herein (see Example 8 of the Exemplification).

15 In addition to the nucleic acid molecules encoding MP proteins described above, another aspect of the invention pertains to isolated nucleic acid molecules which are antisense thereto. An "antisense" nucleic acid comprises a nucleotide sequence which is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded DNA molecule or complementary to an mRNA

20 sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire MP coding strand, or to only a portion thereof. In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an MP protein. The term "coding region" refers to the region of the nucleotide sequence

25 comprising codons which are translated into amino acid residues (*e.g.*, the entire coding region of SEQ ID NO. 1 (RXA02229) comprises nucleotides 1 to 825). In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding MP. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into

30 amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding MP disclosed herein (*e.g.*, the sequences set forth as odd-numbered SEQ ID NOs in the Sequence Listing), antisense

nucleic acids of the invention can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of MP mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or noncoding region of MP mRNA. For

5 example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of MP mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an

10 antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified

15 nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine,

20 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (*v*), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-

25 methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5- oxyacetic acid methylester, uracil-5-oxyacetic acid (*v*), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from

30 the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a cell or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding an MCT protein to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by
5 conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. The antisense molecule can be modified such that it specifically binds to a receptor or an antigen expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecule to a peptide or
10 an antibody which binds to a cell surface receptor or antigen. The antisense nucleic acid molecule can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong prokaryotic, viral, or eukaryotic promoter are preferred.

15 In yet another embodiment, the antisense nucleic acid molecule of the invention is an α -anomeric nucleic acid molecule. An α -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-*o*-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res.* 15:6131-6148) or a
20 chimeric RNA-DNA analogue (Inoue *et al.* (1987) *FEBS Lett.* 215:327-330).

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they
25 have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave MP mRNA transcripts to thereby inhibit translation of MP mRNA. A ribozyme having specificity for an MP-encoding nucleic acid can be designed based upon the nucleotide sequence of an MP DNA disclosed herein (*i.e.*, SEQ ID NO: 1
30 (RXA02229). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an MP-encoding mRNA. See, *e.g.*, Cech *et al.*

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U.S. Patent No. 4,987,071 and Cech *et al.* U.S. Patent No. 5,116,742. Alternatively, MP mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418.

- 5 Alternatively, MP gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of an MP nucleotide sequence (*e.g.*, an MP promoter and/or enhancers) to form triple helical structures that prevent transcription of an MP gene in target cells. See generally, Helene, C. (1991) *Anticancer Drug Des.* 6(6):569-84; Helene, C. *et al.* (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and
10 Maher, L.J. (1992) *Bioassays* 14(12):807-15.

B. Recombinant Expression Vectors and Host Cells

- Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an MP protein (or a portion thereof). As
15 used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of
20 autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to
25 which they are operatively linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors,
30 such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

- The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is
- 5 operatively linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory
- 10 sequence" is intended to include promoters, repressor binding sites, activator binding sites, enhancers and other expression control elements (*e.g.*, terminators, polyadenylation signals, or other elements of mRNA secondary structure). Such regulatory sequences are described, for example, in Goeddel; *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990).
- 15 Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells. Preferred regulatory sequences are, for example, promoters such as *cos*-, *tac*-, *trp*-, *tet*-, *trp-tet*-, *lpp*-, *lac*-, *lpp-lac*-, *lacI^q*-, *T7*-, *T5*-, *T3*-, *gal*-, *trc*-, *ara*-, *SP6*-, *arny*, *SPO2*, λ -*P_R*- or λ *P_L*, which are used preferably in bacteria.
- 20 Additional regulatory sequences are, for example, promoters from yeasts and fungi, such as *ADC1*, *MF α* , *AC*, *P-60*, *CYC1*, *GAPDH*, *TEF*, *rp28*, *ADH*, promoters from plants such as *CaMV/35S*, *SSU*, *OCS*, *lib4*, *usp*, *STLS1*, *B33*, *nos* or *ubiquitin*- or *phaseolin*-promoters. It is also possible to use artificial promoters. It will be appreciated by one of ordinary skill in the art that the design of the expression vector can depend on such
- 25 factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, MP proteins, mutant forms of MP proteins, fusion proteins, etc.).
- 30 The recombinant expression vectors of the invention can be designed for expression of MP proteins in prokaryotic or eukaryotic cells. For example, MP genes can be expressed in bacterial cells such as *C. glutamicum*, insect cells (using baculovirus

expression vectors), yeast and other fungal cells (see Romanos, M.A. *et al.* (1992) "Foreign gene expression in yeast: a review", *Yeast* 8: 423-488; van den Hondel, C.A.M.J.J. *et al.* (1991) "Heterologous gene expression in filamentous fungi" in: More Gene Manipulations in Fungi, J.W. Bennet & L.L. Lasure, eds., p. 396-428: Academic Press: San Diego; and van den Hondel, C.A.M.J.J. & Punt, P.J. (1991) "Gene transfer systems and vector development for filamentous fungi, in: Applied Molecular Genetics of Fungi, Peberdy, J.F. *et al.*, eds., p. 1-28, Cambridge University Press: Cambridge), algae and multicellular plant cells (see Schmidt, R. and Willmitzer, L. (1988) High efficiency *Agrobacterium tumefaciens* -mediated transformation of *Arabidopsis thaliana* leaf and cotyledon explants" *Plant Cell Rep.*: 583-586), or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein but also to the C-terminus or fused within suitable regions in the proteins. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase.

Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith, D.B. and Johnson, K.S. (1988) *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein. In one embodiment, the coding sequence of the MP protein is cloned into a pGEX expression vector to create a vector encoding a fusion protein comprising, from

the N-terminus to the C-terminus, GST-thrombin cleavage site-X protein. The fusion protein can be purified by affinity chromatography using glutathione-agarose resin. Recombinant MP protein unfused to GST can be recovered by cleavage of the fusion protein with thrombin.

- 5 Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann *et al.*, (1988) *Gene* 69:301-315) pLG338, pACYC184, pBR322, pUC18, pUC19, pKC30, pRep4, pHS1, pHS2, pPLc236, pMBL24, pLG200, pUR290, pIN-III113-B1, λ gt11, pBdCl, and pET 11d (Studier *et al.*, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California (1990) 60-89; and
- 10 Pouwels *et al.*, eds. (1985) *Cloning Vectors*. Elsevier: New York IBSN 0 444 904018). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 gn10-lac fusion promoter mediated by a coexpressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by
- 15 host strains BL21(DE3) or HMS174(DE3) from a resident λ prophage harboring a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter. For transformation of other varieties of bacteria, appropriate vectors may be selected. For example, the plasmids pIJ101, pIJ364, pIJ702 and pIJ361 are known to be useful in transforming *Streptomyces*, while plasmids pUB110, pC194, or pBD214 are suited for transformation
- 20 of *Bacillus* species. Several plasmids of use in the transfer of genetic information into *Corynebacterium* include pHM1519, pBL1, pSA77, or pAJ667 (Pouwels *et al.*, eds. (1985) *Cloning Vectors*. Elsevier: New York IBSN 0 444 904018).

- One strategy to maximize recombinant protein expression is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the
- 25 recombinant protein (Gottesman, S., *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California (1990) 119-128). Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in the bacterium chosen for expression, such as *C. glutamicum*
- 30 (Wada *et al.* (1992) *Nucleic Acids Res.* 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the MP protein expression vector is a yeast expression vector. Examples of vectors for expression in yeast *S. cerevisiae* include pYepSec1 (Baldari, *et al.*, (1987) *Embo J.* 6:229-234), , 2 μ , pAG-1, Yep6, Yep13, pEMBLYe23, pMFa (Kurjan and Herskowitz, (1982) *Cell* 30:933-943), pJRY88 (Schultz *et al.*, (1987) 5 *Gene* 54:113-123), and pYES2 (Invitrogen Corporation, San Diego, CA). Vectors and methods for the construction of vectors appropriate for use in other fungi, such as the filamentous fungi, include those detailed in: van den Hondel, C.A.M.J.J. & Punt, P.J. (1991) "Gene transfer systems and vector development for filamentous fungi, in: Applied Molecular Genetics of Fungi, J.F. Peberdy, *et al.*, eds., p. 1-28, Cambridge University Press: Cambridge, and Pouwels *et al.*, eds. (1985) Cloning Vectors. Elsevier: 10 New York (IBSN 0 444 904018).

Alternatively, the MP proteins of the invention can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, Sf 9 cells) include the pAc series (Smith *et al.* 15 (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

In another embodiment, the MP proteins of the invention may be expressed in unicellular plant cells (such as algae) or in plant cells from higher plants (*e.g.*, the spermatophytes, such as crop plants). Examples of plant expression vectors include 20 those detailed in: Becker, D., Kemper, E., Schell, J. and Masterson, R. (1992) "New plant binary vectors with selectable markers located proximal to the left border", *Plant Mol. Biol.* 20: 1195-1197; and Bevan, M.W. (1984) "Binary *Agrobacterium* vectors for plant transformation", *Nucl. Acid. Res.* 12: 8711-8721, and include pLGV23, pGHIac+, pBIN19, pAK2004, and pDH51 (Pouwels *et al.*, eds. (1985) Cloning Vectors. Elsevier: 25 New York IBSN 0 444 904018).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, B. (1987) *Nature* 329:840) and pMT2PC (Kaufman *et al.* (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the 30 expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both

prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.*

- 5 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert *et al.* 10 (1987) *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) *Adv. Immunol.* 43:235-275), in particular promoters of T cell receptors (Winoto and Baltimore (1989) *EMBO J.* 8:729-733) and immunoglobulins (Banerji *et al.* (1983) *Cell* 33:729-740; Queen and Baltimore (1983) *Cell* 33:741-748), neuron-specific promoters (*e.g.*, the neurofilament promoter; Byrne and Ruddle (1989) *PNAS* 86:5473-5477), 15 pancreas-specific promoters (Edlund *et al.* (1985) *Science* 230:912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the α -fetoprotein promoter (Campes and Tilghman (1989) 20 *Genes Dev.* 3:537-546).

- The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an 25 RNA molecule which is antisense to MP mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA.
- 30 The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell

type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see Weintraub, H. *et al.*, Antisense RNA as a molecular tool for genetic analysis, *Reviews - Trends in Genetics*, Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant
5 expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be
10 identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, an MP protein can be expressed in bacterial cells such as *C. glutamicum*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other
15 suitable host cells are known to those of ordinary skill in the art. Microorganisms related to *Corynebacterium glutamicum* which may be conveniently used as host cells for the nucleic acid and protein molecules of the invention are set forth in Table 3.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms
20 "transformation" and "transfection", "conjugation" and "transduction" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.*, linear DNA or RNA (*e.g.*, a linearized vector or a gene construct alone without a vector) or nucleic acid in the form of a vector (*e.g.*, a plasmid, phage, phasmid, phagemid, transposon or other DNA) into a host cell, including calcium phosphate or calcium
25 chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, natural competence, chemical-mediated transfer, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (*Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989*), and other laboratory manuals.
30 For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these

integrants, a gene that encodes a selectable marker (*e.g.*, resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be

5 introduced into a host cell on the same vector as that encoding an MP protein or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

To create a homologous recombinant microorganism, a vector is prepared which

10 contains at least a portion of an MP gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the MP gene. Preferably, this MP gene is a *Corynebacterium glutamicum* MP gene, but it can be a homologue from a related bacterium or even from a mammalian, yeast, or insect source. In a preferred embodiment, the vector is designed such that, upon homologous

15 recombination, the endogenous MP gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous MP gene is mutated or otherwise altered but still encodes functional protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the

20 endogenous MP protein). In the homologous recombination vector, the altered portion of the MP gene is flanked at its 5' and 3' ends by additional nucleic acid of the MP gene to allow for homologous recombination to occur between the exogenous MP gene carried by the vector and an endogenous MP gene in a microorganism. The additional flanking MP nucleic acid is of sufficient length for successful homologous

25 recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see *e.g.*, Thomas, K.R., and Capecchi, M.R. (1987) Cell 51: 503 for a description of homologous recombination vectors). The vector is introduced into a microorganism (*e.g.*, by electroporation) and cells in which the introduced MP gene has homologously recombined with the

30 endogenous MP gene are selected, using art-known techniques.

In another embodiment, recombinant microorganisms can be produced which contain selected systems which allow for regulated expression of the introduced gene.

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For example, inclusion of an MP gene on a vector placing it under control of the lac operon permits expression of the MP gene only in the presence of IPTG. Such regulatory systems are well known in the art.

In another embodiment, an endogenous MP gene in a host cell is disrupted (*e.g.*,
5 by homologous recombination or other genetic means known in the art) such that expression of its protein product does not occur. In another embodiment, an endogenous or introduced MP gene in a host cell has been altered by one or more point mutations, deletions, or inversions, but still encodes a functional MP protein. In still another embodiment, one or more of the regulatory regions (*e.g.*, a promoter, repressor, or
10 inducer) of an MP gene in a microorganism has been altered (*e.g.*, by deletion, truncation, inversion, or point mutation) such that the expression of the MP gene is modulated. One of ordinary skill in the art will appreciate that host cells containing more than one of the described MP gene and protein modifications may be readily produced using the methods of the invention, and are meant to be included in the present
15 invention.

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) an MP protein. Accordingly, the invention further provides methods for producing MP proteins using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of
20 invention (into which a recombinant expression vector encoding an MP protein has been introduced, or into which genome has been introduced a gene encoding a wild-type or altered MP protein) in a suitable medium until MP protein is produced. In another embodiment, the method further comprises isolating MP proteins from the medium or the host cell.

25

C. Isolated MP Proteins

Another aspect of the invention pertains to isolated MP proteins, and biologically active portions thereof. An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material when produced by recombinant DNA
30 techniques, or chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of MP protein in which the protein is separated from cellular components of the cells in which

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it is naturally or recombinantly produced. In one embodiment, the language "substantially free of cellular material" includes preparations of MP protein having less than about 30% (by dry weight) of non-MP protein (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-MP protein, still more preferably less than about 10% of non-MP protein, and most preferably less than about 5% non-MP protein. When the MP protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the protein preparation. The language "substantially free of chemical precursors or other chemicals" includes preparations of MP protein in which the protein is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of MP protein having less than about 30% (by dry weight) of chemical precursors or non-MP chemicals, more preferably less than about 20% chemical precursors or non-MP chemicals, still more preferably less than about 10% chemical precursors or non-MP chemicals, and most preferably less than about 5% chemical precursors or non-MP chemicals. In preferred embodiments, isolated proteins or biologically active portions thereof lack contaminating proteins from the same organism from which the MP protein is derived. Typically, such proteins are produced by recombinant expression of, for example, a *C. glutamicum* MP protein in a microorganism such as *C. glutamicum*.

An isolated MP protein or a portion thereof of the invention can catalyze an enzymatic reaction in an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway, or has one or more of the activities set forth in Table 1. In preferred embodiments, the protein or portion thereof comprises an amino acid sequence which is sufficiently homologous to an amino acid sequence of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) such that the protein or portion thereof maintains the ability to catalyze an enzymatic reaction in an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway. The portion of the protein is preferably a biologically active portion as described herein. In another preferred embodiment, an MP protein of

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the invention has an amino acid sequence set forth as an even-numbered SEQ ID NO: of the Sequence Listing. In yet another preferred embodiment, the MP protein has an amino acid sequence which is encoded by a nucleotide sequence which hybridizes, *e.g.*, hybridizes under stringent conditions, to a nucleotide sequence of the invention (*e.g.*, a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing). In still another preferred embodiment, the MP protein has an amino acid sequence which is encoded by a nucleotide sequence that is at least about 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%, more preferably at least about 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to one of the nucleic acid sequences of the invention, or a portion thereof. Ranges and identity values intermediate to the above-recited values, (*e.g.*, 70-90% identical or 80-95% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper and/or lower limits are intended to be included. The preferred MP proteins of the present invention also preferably possess at least one of the MP activities described herein. For example, a preferred MP protein of the present invention includes an amino acid sequence encoded by a nucleotide sequence which hybridizes, *e.g.*, hybridizes under stringent conditions, to a nucleotide sequence of the invention, and which can catalyze an enzymatic reaction in an amino acid, vitamin, cofactor, nutraceutical, nucleotide, nucleoside, or trehalose metabolic pathway, or which has one or more of the activities set forth in Table 1.

In other embodiments, the MP protein is substantially homologous to an amino acid sequence of the invention (*e.g.*, a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) and retains the functional activity of the protein of one of the amino acid sequences of the invention yet differs in amino acid sequence due to natural variation or mutagenesis, as described in detail in subsection I above. Accordingly, in another embodiment, the MP protein is a protein which comprises an amino acid sequence which is at least about 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%, more preferably at least about 71%, 72%, 73%, 74%, 75%, 76%, 77%,

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78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to an entire amino acid sequence of the invention and which has at least one of the MP activities described herein. Ranges and identity values
5 intermediate to the above-recited values, (*e.g.*, 70-90% identical or 80-95% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper and/or lower limits are intended to be included. In another embodiment, the invention pertains to a full length *C. glutamicum* protein which is substantially homologous to an entire
10 amino acid sequence of the invention.

Biologically active portions of an MP protein include peptides comprising amino acid sequences derived from the amino acid sequence of an MP protein, *e.g.*, an amino acid sequence of an even-numbered SEQ ID NO: of the Sequence Listing or the amino acid sequence of a protein homologous to an MP protein, which include fewer amino
15 acids than a full length MP protein or the full length protein which is homologous to an MP protein, and exhibit at least one activity of an MP protein. Typically, biologically active portions (peptides, *e.g.*, peptides which are, for example, 5, 10, 15, 20, 30, 35, 36, 37, 38, 39, 40, 50, 100 or more amino acids in length) comprise a domain or motif with at least one activity of an MP protein. Moreover, other biologically active portions, in
20 which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the activities described herein. Preferably, the biologically active portions of an MP protein include one or more selected domains/motifs or portions thereof having biological activity.

MP proteins are preferably produced by recombinant DNA techniques. For
25 example, a nucleic acid molecule encoding the protein is cloned into an expression vector (as described above), the expression vector is introduced into a host cell (as described above) and the MP protein is expressed in the host cell. The MP protein can then be isolated from the cells by an appropriate purification scheme using standard protein purification techniques. Alternative to recombinant expression, an MP protein,
30 polypeptide, or peptide can be synthesized chemically using standard peptide synthesis techniques. Moreover, native MP protein can be isolated from cells (*e.g.*, endothelial

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cells), for example using an anti-MP antibody, which can be produced by standard techniques utilizing an MP protein or fragment thereof of this invention.

The invention also provides MP chimeric or fusion proteins. As used herein, an MP "chimeric protein" or "fusion protein" comprises an MP polypeptide operatively
5 linked to a non-MP polypeptide. An "MP polypeptide" refers to a polypeptide having an amino acid sequence corresponding to MP, whereas a "non-MP polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not substantially homologous to the MP protein, *e.g.*, a protein which is different from the MP protein and which is derived from the same or a different organism. Within the
10 fusion protein, the term "operatively linked" is intended to indicate that the MP polypeptide and the non-MP polypeptide are fused in-frame to each other. The non-MP polypeptide can be fused to the N-terminus or C-terminus of the MP polypeptide. For example, in one embodiment the fusion protein is a GST-MP fusion protein in which the MP sequences are fused to the C-terminus of the GST sequences. Such fusion proteins
15 can facilitate the purification of recombinant MP proteins. In another embodiment, the fusion protein is an MP protein containing a heterologous signal sequence at its N-terminus. In certain host cells (*e.g.*, mammalian host cells), expression and/or secretion of an MP protein can be increased through use of a heterologous signal sequence.

Preferably, an MP chimeric or fusion protein of the invention is produced by
20 standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid
25 undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric
30 gene sequence (see, for example, *Current Protocols in Molecular Biology*, eds. Ausubel *et al.* John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). An MP-

encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the MP protein.

Homologues of the MP protein can be generated by mutagenesis, *e.g.*, discrete point mutation or truncation of the MP protein. As used herein, the term "homologue" refers to a variant form of the MP protein which acts as an agonist or antagonist of the activity of the MP protein. An agonist of the MP protein can retain substantially the same, or a subset, of the biological activities of the MP protein. An antagonist of the MP protein can inhibit one or more of the activities of the naturally occurring form of the MP protein, by, for example, competitively binding to a downstream or upstream member of the MP cascade which includes the MP protein. Thus, the *C. glutamicum* MP protein and homologues thereof of the present invention may modulate the activity of one or more metabolic pathways in which MP proteins play a role in this microorganism.

In an alternative embodiment, homologues of the MP protein can be identified by screening combinatorial libraries of mutants, *e.g.*, truncation mutants, of the MP protein for MP protein agonist or antagonist activity. In one embodiment, a variegated library of MP variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of MP variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential MP sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display) containing the set of MP sequences therein. There are a variety of methods which can be used to produce libraries of potential MP homologues from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential MP sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, *e.g.*, Narang, S.A. (1983) *Tetrahedron* 39:3; Itakura *et al.* (1984) *Annu. Rev. Biochem.* 53:323; Itakura *et al.* (1984) *Science* 198:1056; Ike *et al.* (1983) *Nucleic Acid Res.* 11:477.

In addition, libraries of fragments of the MP protein coding can be used to generate a variegated population of MP fragments for screening and subsequent selection of homologues of an MP protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of an MP coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal, C-terminal and internal fragments of various sizes of the MP protein.

Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of MP homologues. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify MP homologues (Arkin and Yourvan (1992) *PNAS* 89:7811-7815; Delgrave *et al.* (1993) *Protein Engineering* 6(3):327-331).

In another embodiment, cell based assays can be exploited to analyze a variegated MP library, using methods well known in the art.

D. Uses and Methods of the Invention

The nucleic acid molecules, proteins, protein homologues, fusion proteins, primers, vectors, and host cells described herein can be used in one or more of the following methods: identification of *C. glutamicum* and related organisms; mapping of genomes of organisms related to *C. glutamicum*; identification and localization of *C.*

glutamicum sequences of interest; evolutionary studies; determination of MP protein regions required for function; modulation of an MP protein activity; modulation of the activity of an MP pathway; and modulation of cellular production of a desired compound, such as a fine chemical.

- 5 The MP nucleic acid molecules of the invention have a variety of uses. First, they may be used to identify an organism as being *Corynebacterium glutamicum* or a close relative thereof. Also, they may be used to identify the presence of *C. glutamicum* or a relative thereof in a mixed population of microorganisms. The invention provides the nucleic acid sequences of a number of *C. glutamicum* genes; by probing the
- 10 extracted genomic DNA of a culture of a unique or mixed population of microorganisms under stringent conditions with a probe spanning a region of a *C. glutamicum* gene which is unique to this organism, one can ascertain whether this organism is present. Although *Corynebacterium glutamicum* itself is not pathogenic to humans, it is related to species which are human pathogens, such as *Corynebacterium diphtheriae*.
- 15 *Corynebacterium diphtheriae* is the causative agent of diphtheria, a rapidly developing, acute, febrile infection which involves both local and systemic pathology. In this disease, a local lesion develops in the upper respiratory tract and involves necrotic injury to epithelial cells; the bacilli secrete toxin which is disseminated through this lesion to distal susceptible tissues of the body. Degenerative changes brought about by the
- 20 inhibition of protein synthesis in these tissues, which include heart, muscle, peripheral nerves, adrenals, kidneys, liver and spleen, result in the systemic pathology of the disease. Diphtheria continues to have high incidence in many parts of the world, including Africa, Asia, Eastern Europe and the independent states of the former Soviet Union. An ongoing epidemic of diphtheria in the latter two regions has resulted in at
- 25 least 5,000 deaths since 1990.

 In one embodiment, the invention provides a method of identifying the presence or activity of *Corynebacterium diphtheriae* in a subject. This method includes detection of one or more of the nucleic acid or amino acid sequences of the invention (e.g., the sequences set forth as odd-numbered or even-numbered SEQ ID NOs, respectively, in

30 the Sequence Listing) in a subject, thereby detecting the presence or activity of *Corynebacterium diphtheriae* in the subject. *C. glutamicum* and *C. diphtheriae* are related bacteria, and many of the nucleic acid and protein molecules in *C. glutamicum*

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are homologous to *C. diphtheriae* nucleic acid and protein molecules, and can therefore be used to detect *C. diphtheriae* in a subject.

The nucleic acid and protein molecules of the invention may also serve as markers for specific regions of the genome. This has utility not only in the mapping of
5 the genome, but also for functional studies of *C. glutamicum* proteins. For example, to identify the region of the genome to which a particular *C. glutamicum* DNA-binding protein binds, the *C. glutamicum* genome could be digested, and the fragments incubated with the DNA-binding protein. Those which bind the protein may be additionally probed with the nucleic acid molecules of the invention, preferably with readily detectable
10 labels; binding of such a nucleic acid molecule to the genome fragment enables the localization of the fragment to the genome map of *C. glutamicum*, and, when performed multiple times with different enzymes, facilitates a rapid determination of the nucleic acid sequence to which the protein binds. Further, the nucleic acid molecules of the invention may be sufficiently homologous to the sequences of related species such that
15 these nucleic acid molecules may serve as markers for the construction of a genomic map in related bacteria, such as *Brevibacterium lactofermentum*.

The MP nucleic acid molecules of the invention are also useful for evolutionary and protein structural studies. The metabolic processes in which the molecules of the invention participate are utilized by a wide variety of prokaryotic and eukaryotic cells;
20 by comparing the sequences of the nucleic acid molecules of the present invention to those encoding similar enzymes from other organisms, the evolutionary relatedness of the organisms can be assessed. Similarly, such a comparison permits an assessment of which regions of the sequence are conserved and which are not, which may aid in determining those regions of the protein which are essential for the functioning of the
25 enzyme. This type of determination is of value for protein engineering studies and may give an indication of what the protein can tolerate in terms of mutagenesis without losing function.

Manipulation of the MP nucleic acid molecules of the invention may result in the production of MP proteins having functional differences from the wild-type MP
30 proteins. These proteins may be improved in efficiency or activity, may be present in greater numbers in the cell than is usual, or may be decreased in efficiency or activity.

The invention also provides methods for screening molecules which modulate the activity of an MP protein, either by interacting with the protein itself or a substrate or binding partner of the MP protein, or by modulating the transcription or translation of an MP nucleic acid molecule of the invention. In such methods, a microorganism
5 expressing one or more MP proteins of the invention is contacted with one or more test compounds, and the effect of each test compound on the activity or level of expression of the MP protein is assessed.

When the desired fine chemical to be isolated from large-scale fermentative culture of *C. glutamicum* is an amino acid, a vitamin, a cofactor, a nutraceutical, a
10 nucleotide, a nucleoside, or trehalose, modulation of the activity or efficiency of activity of one or more of the proteins of the invention by recombinant genetic mechanisms may directly impact the production of one of these fine chemicals. For example, in the case of an enzyme in a biosynthetic pathway for a desired amino acid, improvement in efficiency or activity of the enzyme (including the presence of multiple copies of the
15 gene) should lead to an increased production or efficiency of production of that desired amino acid. In the case of an enzyme in a biosynthetic pathway for an amino acid whose synthesis is in competition with the synthesis of a desired amino acid, any decrease in the efficiency or activity of this enzyme (including deletion of the gene) should result in an increase in production or efficiency of production of the desired amino acid, due to
20 decreased competition for intermediate compounds and/or energy. In the case of an enzyme in a degradation pathway for a desired amino acid, any decrease in efficiency or activity of the enzyme should result in a greater yield or efficiency of production of the desired product due to a decrease in its degradation. Lastly, mutagenesis of an enzyme involved in the biosynthesis of a desired amino acid such that this enzyme is no longer is
25 capable of feedback inhibition should result in increased yields or efficiency of production of the desired amino acid. The same should apply to the biosynthetic and degradative enzymes of the invention involved in the metabolism of vitamins, cofactors, nutraceuticals, nucleotides, nucleosides and trehalose.

Similarly, when the desired fine chemical is not one of the aforementioned
30 compounds, the modulation of activity of one of the proteins of the invention may still impact the yield and/or efficiency of production of the compound from large-scale culture of *C. glutamicum*. The metabolic pathways of any organism are closely

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interconnected; the intermediate used by one pathway is often supplied by a different pathway. Enzyme expression and function may be regulated based on the cellular levels of a compound from a different metabolic process, and the cellular levels of molecules necessary for basic growth, such as amino acids and nucleotides, may critically affect

5 the viability of the microorganism in large-scale culture. Thus, modulation of an amino acid biosynthesis enzyme, for example, such that it is no longer responsive to feedback inhibition or such that it is improved in efficiency or turnover may result in increased cellular levels of one or more amino acids. In turn, this increased pool of amino acids provides not only an increased supply of molecules necessary for protein synthesis, but

10 also of molecules which are utilized as intermediates and precursors in a number of other biosynthetic pathways. If a particular amino acid had been limiting in the cell, its increased production might increase the ability of the cell to perform numerous other metabolic reactions, as well as enabling the cell to more efficiently produce proteins of all kinds, possibly increasing the overall growth rate or survival ability of the cell in

15 large scale culture. Increased viability improves the number of cells capable of producing the desired fine chemical in fermentative culture, thereby increasing the yield of this compound. Similar processes are possible by the modulation of activity of a degradative enzyme of the invention such that the enzyme no longer catalyzes, or catalyzes less efficiently, the degradation of a cellular compound which is important for

20 the biosynthesis of a desired compound, or which will enable the cell to grow and reproduce more efficiently in large-scale culture. It should be emphasized that optimizing the degradative activity or decreasing the biosynthetic activity of certain molecules of the invention may also have a beneficial effect on the production of certain fine chemicals from *C. glutamicum*. For example, by decreasing the efficiency of

25 activity of a biosynthetic enzyme in a pathway which competes with the biosynthetic pathway of a desired compound for one or more intermediates, more of those intermediates should be available for conversion to the desired product. A similar situation may call for the improvement of degradative ability or efficiency of one or more proteins of the invention.

30 This aforementioned list of mutagenesis strategies for MP proteins to result in increased yields of a desired compound is not meant to be limiting; variations on these mutagenesis strategies will be readily apparent to one of ordinary skill in the art. By

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these mechanisms, the nucleic acid and protein molecules of the invention may be utilized to generate *C. glutamicum* or related strains of bacteria expressing mutated MP nucleic acid and protein molecules such that the yield, production, and/or efficiency of production of a desired compound is improved. This desired compound may be any

5 natural product of *C. glutamicum*, which includes the final products of biosynthesis pathways and intermediates of naturally-occurring metabolic pathways, as well as molecules which do not naturally occur in the metabolism of *C. glutamicum*, but which are produced by a *C. glutamicum* strain of the invention.

This invention is further illustrated by the following examples which should not

10 be construed as limiting. The contents of all references, patent applications, patents, published patent applications, Tables, and the sequence listing cited throughout this application are hereby incorporated by reference.

TABLE 1: Included Genes

Lysine biosynthesis

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
1	2	RXA02229	GR00653	2793	3617	DIAMINOPIMELATE EPIMERASE (EC 5.1.1.7)
3	4	RXS02970				ACETYLORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
5	6	F RXA01009	GR00287	4714	5943	ACETYLORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
7	8	RXC02390				MEMBRANE SPANNING PROTEIN INVOLVED IN LYSINE METABOLISM
9	10	RXC01796				MEMBRANE ASSOCIATED PROTEIN INVOLVED IN LYSINE METABOLISM
11	12	RXC01207				CYTOSOLIC PROTEIN INVOLVED IN METABOLISM OF LYSINE AND THREONINE
13	14	RXC00657				TRANSCRIPTIONAL REGULATOR INVOLVED IN LYSINE METABOLISM
15	16	RXC00552				CYTOSOLIC PROTEIN INVOLVED IN LYSINE METABOLISM

Trehalose

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
17	18	RXN00351	VV0135	37078	38532	ALPHA ALPHA-TREHALOSE-PHOSPHATE SYNTHASE (UDP-FORMING) 56 KD SUBUNIT (EC 2.4.1.15)
19	20	F RXA00351	GR00066	1486	2931	ALPHA ALPHA-TREHALOSE-PHOSPHATE SYNTHASE (UDP-FORMING) 56 KD SUBUNIT (EC 2.4.1.15)
21	22	RXA00873	GR00241	3	758	trehalose synthase (EC 2.4.1.-)
23	24	RXA00891	GR00243	1005	4	trehalose synthase (EC 2.4.1.-)

Lysine biosynthesis

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
25	26	RXA00534	GR00137	4758	3496	ASPARTOKINASE ALPHA AND BETA SUBUNITS (EC 2.7.2.4)
27	28	RXA00533	GR00137	3469	2438	ASPARTATE-SEMIALDEHYDE DEHYDROGENASE (EC 1.2.1.11)
29	30	RXA02843	GR00842	543	4	2,3,4,5-TETRAHYDROPYRIDINE-2-CARBOXYLATE N-SUCCINYLTRANSFERASE (EC 2.3.1.117)
31	32	RXA02022	GR00613	2063	3169	SUCCINYL-DIAMINOPIMELATE DESUCCINYLAASE (EC 3.5.1.18)
33	34	RXA00044	GR00007	3458	4393	DIHYDRODIPICOLINATE SYNTHASE (EC 4.2.1.52)
35	36	RXA00863	GR00236	896	1639	DIHYDRODIPICOLINATE REDUCTASE (EC 1.3.1.26)
37	38	RXA00864	GR00236	1694	2443	probable 2,3-dihydrodipicolinate N-C6-lyase (cyclizing) (EC 4.3.3.-) - Corynebacterium glutamicum
39	40	RXA02843	GR00842	543	4	2,3,4,5-TETRAHYDROPYRIDINE-2-CARBOXYLATE N-SUCCINYLTRANSFERASE (EC 2.3.1.117)
41	42	RXN00355	VV0135	31980	30961	MESO-DIAMINOPIMELATE D-DEHYDROGENASE
43	44	F RXA00352	GR00068	861	4	MESO-DIAMINOPIMELATE D-DEHYDROGENASE (EC 1.4.1.16)

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
45	46	RXA00972	GR00274	3	1379	DIAMINOPELMATE DECARBOXYLASE (EC 4.1.1.20)
47	48	RXA02653	GR00752	5237	7234	DIAMINOPELMATE DECARBOXYLASE (EC 4.1.1.20)
49	50	RXA01393	GR00408	4249	3380	LYSINE EXPORT REGULATOR PROTEIN
51	52	RXA00241	GR00036	5443	6945	L-LYSINE TRANSPORT PROTEIN
53	54	RXA01394	GR00408	4320	5018	LYSINE EXPORTER PROTEIN
55	56	RXA00865	GR00236	2647	3549	DIHYDRODIPICOLINATE SYNTHASE (EC 4.2.1.52)
57	58	RXS02021				2,3,4,5-TETRAHYDROPYRIDINE-2-CARBOXYLATE N-SUCCINYLTTRANSFERASE (EC 2.3.1.117)
59	60	RXS02157				ACETYLMORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
61	62	RXC00733				ABC TRANSPORTER ATP-BINDING PROTEIN INVOLVED IN LYSINE METABOLISM
63	64	RXC00861				PROTEIN INVOLVED IN LYSINE METABOLISM
65	66	RXC00866				ZN-DEPENDENT HYDROLASE INVOLVED IN LYSINE METABOLISM
67	68	RXC02095				ABC TRANSPORTER ATP-BINDING PROTEIN INVOLVED IN LYSINE METABOLISM
69	70	RXC03185				PROTEIN INVOLVED IN LYSINE METABOLISM

Glutamate and glutamine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
71	72	RXN00367	VW0196	9744	14273	GLUTAMATE SYNTHASE [NADH] PRECURSOR (EC 1.4.1.14)
73	74	F RXA00007	GR00001	7107	8912	GLUTAMATE SYNTHASE (NADPH) LARGE CHAIN PRECURSOR (EC 1.4.1.13)
75	76	F RXA00364	GR00074	1296	4	GLUTAMATE SYNTHASE (NADPH) LARGE CHAIN PRECURSOR (EC 1.4.1.13)
77	78	F RXA00367	GR00075	1806	964	GLUTAMATE SYNTHASE (NADPH) LARGE CHAIN PRECURSOR (EC 1.4.1.13)
79	80	RXN00076	VW0154	2752	4122	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
81	82	F RXA00075	GR00012	2757	3419	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
83	84	RXN00198	VW0181	7916	7368	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
85	86	F RXA00198	GR00031	2	283	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
87	88	RXN00365	VW0196	14607	15233	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
89	90	F RXA00365	GR00075	630	4	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
91	92	RXA00366	GR00075	961	605	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
93	94	RXA02072	GR00628	1259	2599	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
95	96	RXA00335	GR00057	3855	5192	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
97	98	RXA00324	GR00057	19180	17750	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
99	100	RXA00324	GR00057	5262	8396	GLUTAMATE SYNTHASE (NADPH) SMALL CHAIN (EC 1.4.1.13)
101	102	RXN03176	VW0332	2	862	NADP-SPECIFIC GLUTAMATE DEHYDROGENASE (EC 1.4.1.4)
103	104	F RXA02879	GR10017	2	862	GLUTAMINE SYNTHETASE (EC 6.3.1.2)
105	106	RXA00278	GR00043	2612	1581	GLUTAMATE-AMMONIA-LIGASE ADENYLYLTRANSFERASE (EC 2.7.7.42)
107	108	RXA00727	GR00193	614	1525	GLUTAMINASE (EC 3.5.1.2)
						GLUTAMINE-BINDING PROTEIN PRECURSOR
						GLUTAMINE-BINDING PERIPLASMIC PROTEIN PRECURSOR

Table 1 (continued)
Alanine and Aspartate and Asparagine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
109	110	RXA02139	GR00639	6739	4901	ASPARAGINE SYNTHETASE (GLUTAMINE-HYDROLYZING) (EC 6.3.5.4)
111	112	RXN00116	VW0100	25974	25814	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
113	114	F RXA00116	GR00018	510	4	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
115	116	RXN00618	VW0135	10288	9182	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
117	118	F RXA00618	GR00163	213	746	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
119	120	F RXA00627	GR00164	854	1138	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
121	122	RXA02550	GR00729	1585	275	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
123	124	RXA02193	GR00645	1942	365	ASPARTATE AMONIA-LYASE (EC 4.3.1.1)
125	126	RXA02432	GR00708	2669	1695	L-ASPARAGINASE (EC 3.5.1.1)
127	128	RXN03003	VW0138	680	6	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
129	130	RXN00508	VW0086	4701	5783	ALANINE RACEMASE (EC 5.1.1.1)
131	132	RXN00636	VW0135	20972	19944	ALANINE RACEMASE, BIOSYNTHETIC (EC 5.1.1.1)

beta-Alanine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
133	134	RXA02536	GR00726	8581	7826	BETA-UREIDOPROPIONASE (EC 3.5.1.6)
135	136	RXS00870				METHYLMALONATE-SEMIALDEHYDE DEHYDROGENASE (ACYLATING) (EC 1.2.1.27)
137	138	RXS02299				ASPARTATE 1-DECARBOXYLASE PRECURSOR (EC 4.1.1.11)

Glycine and serine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
139	140	RXA01561	GR00435	1113	2042	L-SERINE DEHYDRATASE (EC 4.2.1.13)
141	142	RXA01850	GR00525	481	1827	L-SERINE DEHYDRATASE (EC 4.2.1.13)
143	144	RXA00580	GR00156	7343	6042	SERINE HYDROXYMETHYLTRANSFERASE (EC 2.1.2.1)
145	146	RXA01821	GR00515	10253	9876	SARCOSINE OXIDASE (EC 1.5.3.1)
147	148	RXN02263	VW0202	11783	12160	SARCOSINE OXIDASE (EC 1.5.3.1)
149	150	F RXA02263	GR00654	33454	33813	SARCOSINE OXIDASE (EC 1.5.3.1)
151	152	RXA02176	GR00641	11454	12581	PHOSPHOSERINE AMINOTRANSFERASE (EC 2.6.1.52)
153	154	RXN02758	GR00766	5082	4648	PHOSPHOSERINE PHOSPHATASE (EC 3.1.3.3)
155	156	F RXA02479	GR00717	393	4	PHOSPHOSERINE PHOSPHATASE (EC 3.1.3.3)
157	158	F RXA02758	GR00766	5082	4648	PHOSPHOSERINE PHOSPHATASE (EC 3.1.3.3)
159	160	F RXA02759	GR00766	5330	5220	PHOSPHOSERINE PHOSPHATASE (EC 3.1.3.3)
161	162	RXA02501	GR00720	15041	13977	PHOSPHOSERINE PHOSPHATASE (EC 3.1.3.3)
163	164	RXN03105	VW0074	15857	15423	SARCOSINE OXIDASE (EC 1.5.3.1)
165	166	RXS01130				D-3-PHOSPHOGLYCERATE DEHYDROGENASE (EC 1.1.1.95)
167	168	RXS03112				D-3-PHOSPHOGLYCERATE DEHYDROGENASE (EC 1.1.1.95)

Table 1 (continued)

Threonine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
169	170	RXN00969	VW0149	12053	13387	HOMOSERINE DEHYDROGENASE (EC 1.1.1.3)
171	172	F RXA00974	GR00274	2623	3015	HOMOSERINE DEHYDROGENASE (EC 1.1.1.3)
173	174	RXA00970	GR00273	161	1087	HOMOSERINE KINASE (EC 2.7.1.39)
175	176	RXA00330	GR00057	12968	14410	THREONINE SYNTHASE (EC 4.2.99.2)
177	178	RXN00403	VW0086	70041	68911	HOMOSERINE O-ACETYLTRANSFERASE
179	180	F RXA00403	GR00088	723	1832	HOMOSERINE O-ACETYLTRANSFERASE (EC 2.3.1.11)
181	182	RXC01207				CYTOSOLIC PROTEIN INVOLVED IN METABOLISM OF LYSINE AND THREONINE
183	184	RXC00152				MEMBRANE ASSOCIATED PROTEIN INVOLVED IN THREONINE METABOLISM

Metabolism of methionine and S-adenosyl methionine

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
185	186	RXA00115	GR00017	5359	4313	HOMOSERINE O-ACETYLTRANSFERASE (EC 2.3.1.31)
187	188	RXN00403	VW0086	70041	68911	HOMOSERINE O-ACETYLTRANSFERASE
189	190	F RXA00403	GR00088	723	1832	HOMOSERINE O-ACETYLTRANSFERASE (EC 2.3.1.11)
191	192	RXS03158				CYSTATHIONINE GAMMA-SYNTHASE (EC 4.2.99.9)
193	194	F RXA00254	GR00038	2404	1811	CYSTATHIONINE GAMMA-SYNTHASE (EC 4.2.99.9)
195	196	RXA02532	GR00726	3085	2039	CYSTATHIONINE GAMMA-SYNTHASE (EC 4.2.99.9)
197	198	RXS03159				CYSTATHIONINE GAMMA-SYNTHASE (EC 4.2.99.9)
199	200	F RXA02768	GR00770	1919	2521	CYSTATHIONINE GAMMA-SYNTHASE (EC 4.2.99.9)
201	202	RXA00216	GR00032	16286	15297	5-methyltetrahydrofolate-homocysteine methyltransferase (methionine synthetase)
203	204	RXN00402	VW0086	70787	70188	O-ACETYLHOMOSERINE SULFHYDRYLASE (EC 4.2.99.10) / O-ACETYL SERINE SULFHYDRYLASE (EC 4.2.99.8)
205	206	F RXA00402	GR00088	1	576	O-ACETYLHOMOSERINE SULFHYDRYLASE (EC 4.2.99.10) / O-ACETYL SERINE SULFHYDRYLASE (EC 4.2.99.8)
207	208	RXA00405	GR00089	3289	3801	O-ACETYLHOMOSERINE SULFHYDRYLASE (EC 4.2.99.10) / O-ACETYL SERINE SULFHYDRYLASE (EC 4.2.99.8)
209	210	RXA02197	GR00645	4552	4025	5-METHYLTETRAHYDROFOLATE-HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.13)
211	212	RXN02198	VW0302	9228	11726	5-METHYLTETRAHYDROFOLATE-HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.13)
213	214	F RXA02198	GR00646	2483	6	5-METHYLTETRAHYDROFOLATE-HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.13)
215	216	RXN03074	VW0042	2238	1741	S-ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE METHYLTRANSFERASE (EC 2.1.1.1)
217	218	F RXA02906	GR10044	1142	645	S-ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE METHYLTRANSFERASE (EC 2.1.1.1)
219	220	RXN00132	VW0124	3612	5045	ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE
221	222	F RXA00132	GR00020	7728	7624	ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
223	224	F RXA01371	GR00398	2339	3634	ADENOSYLHOMOCYSTEINASE (EC 3.3.1.1)
225	226	RXN02085				5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE
227	228	F RXA02085	GR00629	3496	5295	METHYLTRANSFERASE (EC 2.1.1.14)
229	230	F RXA02088	GR00629	5252	5731	5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE
231	232	RXN02648				METHYLTRANSFERASE (EC 2.1.1.14)
233	234	F RXA02648	GR00751	5254	4730	5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE
235	236	F RXA02658	GR00752	14764	15447	METHYLTRANSFERASE (EC 2.1.1.14)
237	238	RXC02238				5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE
239	240	RXC00128				METHYLTRANSFERASE (EC 2.1.1.14)
						PROTEIN INVOLVED IN METABOLISM OF S-ADENOSYLMETHIONINE, PURINES AND PANTOTHENATE
						EXPORTED PROTEIN INVOLVED IN METABOLISM OF PYRIDIMES AND ADENOSYLHOMOCYSTEINE

S-adenosyl methionine (SAM) Biosynthesis

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
241	242	RXA02240	GR00654	7160	8380	S-ADENOSYLMETHIONINE SYNTHETASE (EC 2.5.1.6)

Cysteine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
243	244	RXA00780	GR00206	1689	2234	SERINE ACETYLTRANSFERASE (EC 2.3.1.30)
245	246	RXA00779	GR00206	550	1482	CYSTEINE SYNTHASE (EC 4.2.99.8)
247	248	RXN00402	WV0086	70787	70188	O-ACETYLHOMOSERINE SULFHYDRYLASE (EC 4.2.99.10) / O-ACETYL SERINE SULFHYDRYLASE (EC 4.2.99.8)
249	250	F RXA00402	GR00088	1	576	O-ACETYLHOMOSERINE SULFHYDRYLASE (EC 4.2.99.10) / O-ACETYL SERINE SULFHYDRYLASE (EC 4.2.99.8)
251	252	RXS00405				O-ACETYLHOMOSERINE SULFHYDRYLASE (EC 4.2.99.10) / O-ACETYL SERINE SULFHYDRYLASE (EC 4.2.99.8)
253	254	RXC00164				ABC TRANSPORTER ATP-BINDING PROTEIN INVOLVED IN CYSTEINE METABOLISM
255	256	RXC01191				ABC TRANSPORTER ATP-BINDING PROTEIN INVOLVED IN CYSTEINE METABOLISM

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Table 1 (continued)

Valine, leucine and isoleucine

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
257	258	RXA02646	GR00751	3856	2588	THREONINE DEHYDRATASE BIOSYNTHETIC (EC 4.2.1.16)
259	260	RXA00766	GR00204	5091	4249	BRANCHED-CHAIN AMINO ACID AMINOTRANSFERASE (EC 2.6.1.42)
261	262	RXN01690	VV0246	1296	196	BRANCHED-CHAIN AMINO ACID AMINOTRANSFERASE (EC 2.6.1.42)
263	264	F RXA01690	GR00473	1248	196	BRANCHED-CHAIN AMINO ACID AMINOTRANSFERASE (EC 2.6.1.42)
265	266	RXN01026	VV0143	9171	7513	3-ISOPROPYLMALATE DEHYDRATASE LARGE SUBUNIT (EC 4.2.1.33)
267	268	F RXA01026	GR00294	1	1602	3-ISOPROPYLMALATE DEHYDRATASE LARGE SUBUNIT (EC 4.2.1.33)
269	270	RXN01127	VV0157	4491	3472	3-ISOPROPYLMALATE DEHYDROGENASE (EC 1.1.1.85)
271	272	F RXA01132	GR00315	1349	1651	3-ISOPROPYLMALATE DEHYDROGENASE (EC 1.1.1.85)
273	274	RXN00536	VV0219	6128	7498	2-ISOPROPYLMALATE SYNTHASE (EC 4.1.3.12)
275	276	F RXA00536	GR00137	6128	7360	2-ISOPROPYLMALATE SYNTHASE (EC 4.1.3.1)
277	278	RXN02965	VV0143	7711	7121	3-ISOPROPYLMALATE DEHYDRATASE SMALL SUBUNIT (EC 4.2.1.33)
279	280	RXN01929	VV0127	47590	48402	3-METHYL-2-OXOBUTANOATE HYDROXYMETHYLTRANSFERASE (EC 2.1.2.11)
281	282	F RXA01929	GR00555	2766	1960	/ DECARBOXYLASE (EC 4.1.1.44)
283	284	RXN01420	VV0122	15584	14643	3-METHYL-2-OXOBUTANOATE HYDROXYMETHYLTRANSFERASE (EC 2.1.2.11)
285	286	RXS01145				4"-MYCAROSYL ISOVALERYL-COA TRANSFERASE (EC 2.---)
287	288	F RXA01145	GR00321	1075	1530	KETOL-ACID REDUCTOISOMERASE (EC 1.1.1.86)
						KETOL-ACID REDUCTOISOMERASE (EC 1.1.1.86)

Arginine and proline metabolism

Enzymes of proline biosynthesis:

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
289	290	RXA02375	GR00689	1449	223	GLUTAMATE 5-KINASE (EC 2.7.2.11)
291	292	RXN02382	VV0213	5162	3867	GAMMA-GLUTAMYL PHOSPHATE REDUCTASE (GPR) (EC 1.2.1.41)
293	294	F RXA02378	GR00690	624	16	GAMMA-GLUTAMYL PHOSPHATE REDUCTASE (GPR) (EC 1.2.1.41)
295	296	F RXA02382	GR00691	2493	1894	GAMMA-GLUTAMYL PHOSPHATE REDUCTASE (GPR) (EC 1.2.1.41)
297	298	RXA02499	GR00720	11883	12692	PYRROLINE-5-CARBOXYLATE REDUCTASE (EC 1.5.1.2)
299	300	RXS02157				ACETYLRNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
301	302	RXS02262				ORNITHINE CYCLODEAMINASE (EC 4.3.1.12)
303	304	RXS02970				ACETYLRNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
305	306	F RXA01009	GR00287	4714	5943	ACETYLRNITHINE AMINOTRANSFERASE (EC 2.6.1.11)

Table 1 (continued)

Enzymes of proline degradation:

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
307	308	RXN00023	VV0127	68158	64703	PROLINE DEHYDROGENASE (EC 1.5.99.8) / DELTA-1- PYRROLINE-5-CARBOXYLATE DEHYDROGENASE (EC 1.5.1.12)
309	310	F RXA00023	GR00003	2	454	PROLINE DEHYDROGENASE (EC 1.5.99.8) / DELTA-1- PYRROLINE-5-CARBOXYLATE DEHYDROGENASE (EC 1.5.1.12)
311	312	F RXA02284	GR00660	3028	5	PROLINE DEHYDROGENASE (EC 1.5.99.8) / DELTA-1- PYRROLINE-5-CARBOXYLATE DEHYDROGENASE (EC 1.5.1.12)
313	314	RXC02498				PROTEIN INVOLVED IN PROLINE METABOLISM

Synthesis of 3-Hydroxy-proline:

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
315	316	RXA01491	GR00423	5337	4687	DNA FOR L-PROLINE 3-HYDROXYLASE, COMPLETE CDS

Enzymes of ornithine, arginine and spermidine metabolism:

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
317	318	RXA02155	GR00640	1913	3076	GLUTAMATE N-ACETYLTRANSFERASE (EC 2.3.1.35) / AMINO-ACID ACETYLTRANSFERASE (EC 2.3.1.1)
319	320	RXA02156	GR00640	3125	4075	ACETYLGLUTAMATE KINASE (EC 2.7.2.8)
321	322	RXN02153	VV0122	14106	13327	N-ACETYL-GAMMA-GLUTAMYL-PHOSPHATE REDUCTASE (EC 1.2.1.38)
323	324	F RXA02153	GR00640	757	1536	N-ACETYLGLUTAMATE-5-SEMIALDEHYDE DEHYDROGENASE
325	326	RXA02154	GR00640	1536	1826	N-ACETYLGLUTAMATE-5-SEMIALDEHYDE DEHYDROGENASE
327	328	RXA02157	GR00640	4079	5251	ACETYLORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
329	330	RXS02970				ACETYLORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
331	332	F RXA01009	GR00287	4714	5943	ACETYLORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
333	334	RXA02158	GR00640	5268	6224	ORNITHINE CARBAMOYLTRANSFERASE (EC 2.6.1.11)
335	336	RXA02160	GR00640	6914	8116	ORNITHINE CARBAMOYLTRANSFERASE (EC 2.6.1.11)
337	338	RXN02162	VV0122	5683	5253	ARGININOSUCCINATE SYNTHASE (EC 6.3.4.5)
339	340	F RXA02161	GR00640	8180	8962	ARGININOSUCCINATE LYASE (EC 4.3.2.1)
341	342	F RXA02162	GR00640	8949	9611	ARGININOSUCCINATE LYASE (EC 4.3.2.1)
343	344	RXA02262	GR00654	32291	33436	ORNITHINE CYCLODEAMINASE (EC 4.3.1.12)
345	346	RXA00219	GR00032	19289	20230	SPERMIDINE SYNTHASE (EC 2.5.1.16)
347	348	RXA01508	GR00424	12652	14190	SPERMIDINE SYNTHASE (EC 2.5.1.16)
349	350	RXA01757	GR00498	2942	2142	PUTRESCINE OXIDASE (EC 1.4.3.10)
351	352	RXA02159	GR00640	6231	6743	ARGININE HYDROXIMATE RESISTANCE PROTEIN
353	354	RXN02154	VV0122	13327	13037	N-ACETYL-GAMMA-GLUTAMYL-PHOSPHATE REDUCTASE (EC 1.2.1.38)
355	356	RXS00147				CARBAMOYL-PHOSPHATE SYNTHASE SMALL CHAIN (EC 6.3.5.5)
357	358	RXS00905				N-ACYL-L-AMINO ACID AMIDOHYDROLASE (EC 3.5.1.14)
359	360	RXS00906				N-ACYL-L-AMINO ACID AMIDOHYDROLASE (EC 3.5.1.14)

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
361	362	RXS00907				N-ACYL-L-AMINO ACID AMIDOHYDROLASE (EC 3.5.1.14)
363	364	RXS02001				N-ACYL-L-AMINO ACID AMIDOHYDROLASE (EC 3.5.1.14)
365	366	RXS02101				N-ACYL-L-AMINO ACID AMIDOHYDROLASE (EC 3.5.1.14)
367	368	RXS02234				CARBAMOYL-PHOSPHATE SYNTHASE LARGE CHAIN (EC 6.3.5.5)
369	370	F RXA02234	GR00654	1	3198	CARBAMOYL-PHOSPHATE SYNTHASE LARGE CHAIN (EC 6.3.5.5)
371	372	RXS02565				N-ACYL-L-AMINO ACID AMIDOHYDROLASE (EC 3.5.1.14)
373	374	RXS02937				N-ACYL-L-AMINO ACID AMIDOHYDROLASE (EC 3.5.1.14)

Histidine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
375	376	RXA02194	GR00645	2897	2055	ATP PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.17)
377	378	RXA02195	GR00645	3186	2917	PHOSPHORIBOSYL-ATP PYROPHOSPHOHYDROLASE (EC 3.6.1.31)
379	380	RXA01097	GR00306	4726	4373	PHOSPHORIBOSYL-AMP CYCLOHYDROLASE (EC 3.5.4.19)
381	382	RXA01100	GR00306	7072	6335	PHOSPHORIBOSYLFORMIMINO-5-AMINOIMIDAZOLE CARBOXAMIDE RIBOTIDE ISOMERASE (EC 5.3.1.16)
383	384	RXA01101	GR00306	7726	7094	AMIDOTRANSFERASE HISH (EC 2.4.2.-)
385	386	RXN01657	VV0010	39950	39351	AMIDOTRANSFERASE HISH (EC 2.4.2.-)
387	388	F RXA01657	GR00460	2444	2944	AMIDOTRANSFERASE HISH (EC 2.4.2.-)
389	390	RXA01098	GR00306	5499	4726	HISF PROTEIN
391	392	RXN01104	VV0059	7037	6432	IMIDAZOLEGLYCEROL-PHOSPHATE DEHYDRATASE (EC 4.2.1.19)
393	394	F RXA01104	GR00306	10927	10322	IMIDAZOLEGLYCEROL-PHOSPHATE DEHYDRATASE (EC 4.2.1.19) / HISTIDINOL-PHOSPHATASE (EC 3.1.3.15)
395	396	RXN00446	VV0112	24181	23318	HISTIDINOL-PHOSPHATE AMINOTRANSFERASE (EC 2.6.1.9)
397	398	F RXA00446	GR00108	4	525	HISTIDINOL-PHOSPHATE AMINOTRANSFERASE (EC 2.6.1.9)
399	400	RXA01105	GR00306	12044	10947	HISTIDINOL-PHOSPHATE AMINOTRANSFERASE (EC 2.6.1.9)
401	402	RXA01106	GR00306	13378	12053	HISTIDINOL DEHYDROGENASE (EC 1.1.1.23)
403	404	RXC00930				PROTEIN INVOLVED IN HISTIDINE METABOLISM
405	406	RXC01096				PROTEIN INVOLVED IN HISTIDINE METABOLISM
407	408	RXC01656				PROTEIN INVOLVED IN HISTIDINE METABOLISM
409	410	RXC01158				MEMBRANE SPANNING PROTEIN INVOLVED IN HISTIDINE METABOLISM

Metabolism of aromatic amino acids

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
411	412	RXA02458	GR00712	3056	4345	3-PHOSPHOSHAKIMATE 1-CARBOXYVINYLTRANSFERASE (EC 2.5.1.19)
413	414	RXA02790	GR00777	5806	6948	4-AMINO-4-DEOXYCHORISMATE LYASE (EC 4.-.-)
415	416	RXN00954	VV0247	3197	2577	ANTHRANILATE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.18)
417	418	F RXA00954	GR00263	3	590	ANTHRANILATE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.18)
419	420	RXN00957	VV0208	1211	2764	ANTHRANILATE SYNTHASE COMPONENT I (EC 4.1.3.27)
421	422	F RXA00957	GR00264	3	1130	ANTHRANILATE SYNTHASE COMPONENT I (EC 4.1.3.27)

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
423	424	RXA02687	GR00754	11306	12250	CHORISMATE MUTASE (EC 5.4.99.5) / PREPHENATE DEHYDRATASE (EC 4.2.1.51)
425	426	RXN01698	VW0134	11507	12736	CHORISMATE SYNTHASE (EC 4.6.1.4)
427	428	F RXA01698	GR00477	2	991	CHORISMATE SYNTHASE (EC 4.6.1.4)
429	430	RXA01095	GR00306	3603	2821	INDOLE-3-GLYCEROL PHOSPHATE SYNTHASE (EC 4.1.1.48)
431	432	RXA00955	GR00263	586	2007	INDOLE-3-GLYCEROL PHOSPHATE SYNTHASE (EC 4.1.1.48) / N-(5-PHOSPHO-RIBOSYL)ANTHRANILATE ISOMERASE (EC 5.3.1.24)
433	434	RXA02814	GR00795	598	128	ISOCHORISMATE MUTASE
435	436	RXA00229	GR00033	1715	936	SHIKIMATE 5-DEHYDROGENASE (EC 1.1.1.25)
437	438	RXA02093	GR00629	12444	13247	SHIKIMATE 5-DEHYDROGENASE (EC 1.1.1.25)
439	440	RXA02791	GR00777	6968	7795	SHIKIMATE 5-DEHYDROGENASE (EC 1.1.1.25)
441	442	RXA01699	GR00477	984	1553	SHIKIMATE KINASE (EC 2.7.1.71)
443	444	RXA00952	GR00262	97	936	TRYPTOPHAN SYNTHASE ALPHA CHAIN (EC 4.2.1.20)
445	446	RXN00956	VW0247	1140	4	TRYPTOPHAN SYNTHASE BETA CHAIN (EC 4.2.1.20)
447	448	F RXA00956	GR00263	2027	3157	TRYPTOPHAN SYNTHASE BETA CHAIN (EC 4.2.1.20)
449	450	RXA00064	GR00010	2499	3776	TYROSINE AMINOTRANSFERASE (EC 2.6.1.5)
451	452	RXN00448	GR00112	33959	32940	PREPHENATE DEHYDROGENASE (EC 1.3.1.12)
453	454	F RXA00448	GR00109	3	668	PREPHENATE DEHYDROGENASE (EC 1.3.1.12)
455	456	F RXA00452	GR00110	854	1099	PREPHENATE DEHYDROGENASE (EC 1.3.1.12)
457	458	RXA00584	GR00156	11384	10260	PHOSPHO-2-DEHYDRO-3-DEOXYHEPTONATE ALDOLASE (EC 4.1.2.15)
459	460	RXA00579	GR00156	5946	4087	PARA-AMINOBENZOATE SYNTHASE COMPONENT I (EC 4.1.3.-)
461	462	RXA00958	GR00264	1130	1753	PARA-AMINOBENZOATE SYNTHASE GLUTAMINE AMIDOTRANSFERASE COMPONENT II (EC 4.1.3.-) / ANTHRANILATE SYNTHASE COMPONENT II (EC 4.1.3.27)
463	464	RXN03007	VW0208	3410	3778	ANTHRANILATE SYNTHASE COMPONENT II (EC 4.1.3.27)
465	466	RXN02918	VW0086	25447	25887	TRYPTOPHAN SYNTHASE BETA CHAIN (EC 4.2.1.20)
467	468	RXN01116	VW0182	7497	6886	3-OXOADIPATE COA-TRANSFERASE SUBUNIT B (EC 2.8.3.6)
469	470	RXN01115	VW0182	10347	11099	3-OXOADIPATE ENOL-LACTONE HYDROLASE (EC 3.1.1.24) / 4-CARBOXYMUCONOLACTONE
471	472	RXS00116	GR00018	510	4	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
473	474	F RXA00116	GR00018	510	4	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
475	476	RXS00391				O-SUCCINYL-BENZOIC ACID-COA LIGASE (EC 6.2.1.26)
477	478	RXS00393				1,4-DIHYDROXY-2-NAPHTHOATE OCTAPRENYLTRANSFERASE (EC 2.5.-.-)
479	480	F RXA00393	GR00086	4030	4911	1,4-DIHYDROXY-2-NAPHTHOATE OCTAPRENYLTRANSFERASE (EC 2.5.-.-)
481	482	RXS00446	GR00108	4	525	HISTIDINOL-PHOSPHATE AMINOTRANSFERASE (EC 2.6.1.9)
483	484	F RXA00446	GR00108	4	525	HISTIDINOL-PHOSPHATE AMINOTRANSFERASE (EC 2.6.1.9)
485	486	RXS00618	GR00163	213	746	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
487	488	F RXA00618	GR00163	213	746	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
489	490	F RXA00627	GR00164	854	1138	ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
491	492	RXS01105				HISTIDINOL-PHOSPHATE AMINOTRANSFERASE (EC 2.6.1.9)
493	494	RXS02315				2-SUCCINYL-6-HYDROXY-2,4-CYCLOHEXADIENE-1-CARBOXYLATE SYNTHASE / 2-OXOGlutarate decarboxylase (EC 4.1.1.71)
495	496	RXS02550				ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
497	498	RXS02319				NAPHTHOATE SYNTHASE (EC 4.1.3.36)
499	500	RXS02908				O-SUCCINYL-BENZOIC ACID-COA LIGASE (EC 6.2.1.26)
501	502	RXS03003				ASPARTATE AMINOTRANSFERASE (EC 2.6.1.1)
503	504	RXS03026				3-DEHYDROQUINATE DEHYDRATASE (EC 4.2.1.10)

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
505	506	RXS03074				S-ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE METHYLTRANSFERASE (EC 2.1.-.-)
507	508	RXC01434				MEMBRANE SPANNING PROTEIN INVOLVED IN METABOLISM OF AROMATIC AMINO ACIDS AND RIBOFLAVIN
509	510	RXC02080				MEMBRANE SPANNING PROTEIN INVOLVED IN METABOLISM OF AROMATIC AMINO ACIDS
511	512	RXC02789				CYTOSOLIC PROTEIN INVOLVED IN METABOLISM OF AROMATIC AMINO ACIDS
513	514	RXC02295				MEMBRANE SPANNING PROTEIN INVOLVED IN METABOLISM OF AROMATIC AMINO ACIDS

Aminobutyrate metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
515	516	RXN03063	VV0035	666	1697	4-aminobutyrate aminotransferase (EC 2.6.1.19)
517	518	RXN02970	VV0021	4714	6081	ACETYLORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)
519	520	F RXA01009	GR00287	4714	5943	ACETYLORNITHINE AMINOTRANSFERASE (EC 2.6.1.11)

Vitamins, vitamin-like substances (cofactors), nutraceuticals

Thiamine metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
521	522	RXA01551	GR00431	2945	4819	THIAMIN BIOSYNTHESIS PROTEIN THIC
523	524	RXA01019	GR00291	6	995	THIAMIN-MONOPHOSPHATE KINASE (EC 2.7.4.16)
525	526	RXA01352	GR00393	609	4	THIAMIN-PHOSPHATE PYROPHOSPHORYLASE (EC 2.5.1.3)
527	528	RXA01381	GR00403	3206	2286	THIF PROTEIN
529	530	RXA01360	GR00394	162	4	THIG PROTEIN
531	532	RXA01361	GR00394	983	378	THIG PROTEIN
533	534	RXA01208	GR00348	229	1032	HYDROXYETHYLTHIAZOLE KINASE (EC 2.7.1.50)
535	536	RXA00838	GR00227	1532	633	APBA PROTEIN
537	538	RXA02400	GR00699	1988	2557	THIAMIN BIOSYNTHESIS PROTEIN X
539	540	RXN01209	VV0270	1019	2446	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
541	542	F RXA01209	GR00348	1019	2446	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
543	544	RXN01413	VV0050	27306	27905	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
545	546	RXN01617	VV0050	22187	22858	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
547	548	F RXA01617	GR00451	2	616	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
549	550	RXS01807				PYRIDOXINE KINASE (EC 2.7.1.35)
551	552	RXC01021				CYTOSOLIC KINASE INVOLVED IN METABOLISM OF SUGARS AND THIAMIN

Table 1 (continued)

Riboflavin metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
553	554	RXN02246	W0130	4388	5371	diaminohydroxyphosphoribosylaminopyrimidine deaminase (EC 3.5.4.26) / 5-amino-6-(5-phosphoribosylamino)uracil reductase (EC 1.1.1.193)
555	556	F RXA02246	GR00654	14299	15282	RIBG PROTEIN riboflavin-specific deaminase (EC 3.5.4.-)
557	558	RXA02247	GR00654	15286	15918	RIBOFLAVIN SYNTHASE ALPHA CHAIN (EC 2.5.1.9)
559	560	RXN02248	W0130	6021	7286	GTP CYCLOHYDROLASE II (EC 3.5.4.25) / 3,4-DIHYDROXY-2-BUTANONE 4-PHOSPHATE SYNTHASE
561	562	F RXA02248	GR00654	15932	17197	RIBA PROTEIN - GTP cyclohydrolase II (EC 3.5.4.25)
563	564	RXN02249	W0130	7301	7777	6,7-DIMETHYL-8-RIBITYLLUMAZINE SYNTHASE (EC 2.5.1.9)
565	566	F RXA02249	GR00654	17212	17688	RIBH PROTEIN - 6,7-dimethyl-8-ribityllumazine synthase (dmrl synthase, lumazine synthase, riboflavin synthase beta chain) [EC:2.5.1.9]
567	568	RXA02250	GR00654	17778	18356	RIBX PROTEIN
569	570	RXA01489	GR00423	3410	2388	RIBOFLAVIN KINASE (EC 2.7.1.26) / FMN ADENYLYLTRANSFERASE (EC 2.7.7.2)
571	572	RXA02135	GR00639	2809	1736	NICOTINATE-NUCLEOTIDE--DIMETHYLBENZIMIDAZOLE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.21)
573	574	RXA01489	GR00423	3410	2388	RIBOFLAVIN KINASE (EC 2.7.1.26) / FMN ADENYLYLTRANSFERASE (EC 2.7.7.2)
575	576	RXN01712	W0191	8993	8298	RIBOFLAVIN-SPECIFIC DEAMINASE (EC 3.5.4.-)
577	578	F RXA01712	GR00484	2652	2152	RIBOFLAVIN-SPECIFIC DEAMINASE (EC 3.5.4.-)
579	580	RXN02384	W0213	1386	679	ALPHA-RIBAZOLE-5-PHOSPHATE PHOSPHATASE (EC 3.1.3.-)
581	582	RXN01560	W0319	767	438	RIBOFLAVIN-SPECIFIC DEAMINASE (EC 3.5.4.-)
583	584	RXN00667	W0109	1363	350	DRAP DEAMINASE
585	586	RXC01711				MEMBRANE SPANNING PROTEIN INVOLVED IN RIBOFLAVIN METABOLISM
587	588	RXC02380				PROTEIN INVOLVED IN RIBOFLAVIN METABOLISM
589	590	F RXA02380	GR00691	709	56	Predicted nucleosideyltransferases
591	592	RXC02921				CYTOSOLIC PROTEIN INVOLVED IN METABOLISM OF RIBOFLAVIN AND LIPIDS
593	594	RXC01434				MEMBRANE SPANNING PROTEIN INVOLVED IN METABOLISM OF AROMATIC AMINO ACIDS AND RIBOFLAVIN

Vitamin B6 metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
595	596	RXA01807	GR00509	7868	7077	PYRIDOXINE KINASE (EC 2.7.1.35), pyridoxal/pyridoxine/pyridoxamine kinase

Table 1 (continued)
Nicotinate (nicotinic acid), nicotinamide, NAD and NADP

<u>Nucleic Acid SEQ ID NO</u>	<u>Amino Acid SEQ ID NO</u>	<u>Identification Code</u>	<u>Contig.</u>	<u>NT Start</u>	<u>NT Stop</u>	<u>Function</u>
597	598	RXN02754	VV0084	22564	23901	NICOTINATE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.11)
599	600	F RXA02405	GR00701	774	4	NICOTINATE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.11)
601	602	F RXA02754	GR00766	3	488	NICOTINATE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.11)
603	604	RXA02112	GR00632	5600	6436	NICOTINATE-NUCLEOTIDE PYROPHOSPHORYLASE (CARBOXYLATING) (EC 2.4.2.19)
605	606	RXA02111	GR00632	4310	5593	QUINOLINATE SYNTHETASE A

NAD Biosynthesis

<u>Nucleic Acid SEQ ID NO</u>	<u>Amino Acid SEQ ID NO</u>	<u>Identification Code</u>	<u>Contig.</u>	<u>NT Start</u>	<u>NT Stop</u>	<u>Function</u>
607	608	RXA01073	GR00300	1274	2104	NH(3)-DEPENDENT NAD(+) SYNTHETASE (EC 6.3.5.1)
609	610	RXN02754	VV0084	22564	23901	NICOTINATE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.11)

Pantothenate and Coenzyme A (CoA) biosynthesis

<u>Nucleic Acid SEQ ID NO</u>	<u>Amino Acid SEQ ID NO</u>	<u>Identification Code</u>	<u>Contig.</u>	<u>NT Start</u>	<u>NT Stop</u>	<u>Function</u>
611	612	RXA02299	GR00662	10452	10859	ASPARTATE 1-DECARBOXYLASE PRECURSOR (EC 4.1.1.11)
613	614	RXA01928	GR00555	1957	1121	PANTOATE--BETA-ALANINE LIGASE (EC 6.3.2.1)
615	616	RXN01929	VV0127	47590	48402	3-METHYL-2-OXOBUTANOATE HYDROXYMETHYLTRANSFERASE (EC 2.1.2.11) / DECARBOXYLASE (EC 4.1.1.44)
617	618	F RXA01929	GR00555	2766	1960	3-METHYL-2-OXOBUTANOATE HYDROXYMETHYLTRANSFERASE (EC 2.1.2.11)
619	620	RXA01521	GR00424	25167	25964	PANTOATE--BETA-ALANINE LIGASE (EC 6.3.2.1)
621	622	RXS01145				KETOL-ACID REDUCTOISOMERASE (EC 1.1.1.86)
623	624	F RXA01145	GR00321	1075	1530	KETOL-ACID REDUCTOISOMERASE (EC 1.1.1.86)
625	626	RXA02239	GR00654	5784	7049	DNA/PANTOTHENATE METABOLISM FLAVOPROTEIN
627	628	RXA00581	GR00156	7572	8540	PANTOTHENATE KINASE (EC 2.7.1.33)
629	630	RXS00838				2-DEHYDRO-PANTOATE 2-REDUCTASE (EC 1.1.1.169)
631	632	RXC02238				PROTEIN INVOLVED IN METABOLISM OF S-ADENOSYLMETHIONINE, PURINES AND PANTOTHENATE

Biotin metabolism

<u>Nucleic Acid SEQ ID NO</u>	<u>Amino Acid SEQ ID NO</u>	<u>Identification Code</u>	<u>Contig.</u>	<u>NT Start</u>	<u>NT Stop</u>	<u>Function</u>
633	634	RXN03058	VV0028	8272	8754	BIOTIN SYNTHESIS PROTEIN BIOC

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
635	636	F RXA02903	GR10040	11532	12014	BIOTIN SYNTHESIS PROTEIN BIOC
637	638	RXA00166	GR00025	3650	4309	BIOTIN SYNTHESIS PROTEIN BIOC
639	640	RXA00633	GR00166	3556	2288	ADENOSYLMETHIONINE-8-AMINO-7-OXONONANOATE AMINOTRANSFERASE (EC 2.6.1.62)
641	642	RXA00632	GR00166	2281	1610	DETHIOBIOTIN SYNTHETASE (EC 6.3.3.3)
643	644	RXA00295	GR00047	3407	4408	BIOTIN SYNTHASE (EC 2.8.1.6)
645	646	RXA00223	GR00032	23967	22879	NIFS PROTEIN
647	648	RXN00262	VV0123	16681	15608	NIFS PROTEIN
649	650	F RXA00262	GR00040	79	897	NIFS PROTEIN
651	652	RXN00435	VV0112	10037	11209	NIFS PROTEIN
653	654	F RXA00435	GR00100	3563	2949	NIFS PROTEIN
655	656	F RXA02801	GR00782	438	4	NIFS PROTEIN
657	658	RXA02516	GR00723	1724	2986	NIFS PROTEIN
659	660	RXA02517	GR00723	2989	3435	NIFU PROTEIN

Lipoic Acid

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
661	662	RXA01747	GR00495	2506	3549	LPOIC ACID SYNTHETASE
663	664	RXA01746	GR00495	1614	2366	LPOATE-PROTEIN LIGASE B (EC 6.---)
665	666	RXA02106	GR00632	472	1527	LPOATE-PROTEIN LIGASE A (EC 6.---)
667	668	RXS01183				DIHYDROLIPOAMIDE SUCCINYLTRANSFERASE COMPONENT (E2) OF 2- OXOGLUTARATE DEHYDROGENASE COMPLEX (EC 2.3.1.61)
669	670	RXS01260				LPOAMIDE DEHYDROGENASE COMPONENT (E3) OF BRANCHED-CHAIN ALPHA-KETO ACID DEHYDROGENASE COMPLEX (EC 1.8.1.4)
671	672	RXS01261				LPOAMIDE DEHYDROGENASE COMPONENT (E3) OF BRANCHED-CHAIN ALPHA-KETO ACID DEHYDROGENASE COMPLEX (EC 1.8.1.4)

Folate biosynthesis

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
673	674	RXA02717	GR00758	18281	17400	5,10-METHYLENETETRAHYDROFOLATE REDUCTASE (EC 1.7.99.5)
675	676	RXN02027	VV0296	503	1003	5-FORMYLTETRAHYDROFOLATE CYCLO-LIGASE (EC 6.3.3.2)
677	678	F RXA02027	GR00616	500	6	5-FORMYLTETRAHYDROFOLATE CYCLO-LIGASE (EC 6.3.3.2)
679	680	RXA00106	GR00014	17469	17924	DIHYDROFOLATE REDUCTASE (EC 1.5.1.3)
681	682	RXN01321	VV0082	8668	9788	FORMYLTETRAHYDROFOLATE DEFORMYLASE (EC 3.5.1.10)
683	684	F RXA01321	GR00384	23	559	FORMYLTETRAHYDROFOLATE DEFORMYLASE (EC 3.5.1.10)
685	686	RXA00461	GR00116	428	1279	METHYLENETETRAHYDROFOLATE DEHYDROGENASE (EC 1.5.1.5) / GTP CYCLOHYDROLASE I (EC 3.5.4.16)
687	688	RXA01514	GR00424	20922	21509	METHYLENETETRAHYDROFOLATE CYCLOHYDROLASE (EC 3.5.4.9)
689	690	RXA01516	GR00424	22360	22749	DIHYDRONEOPTERIN ALDOLASE (EC 4.1.2.25)

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
691	692	RXA01515	GR00424	21513	22364	DIHYDROPTEROATE SYNTHASE (EC 2.5.1.15)
693	694	RXA02024	GR00613	4026	4784	DIHYDROPTEROATE SYNTHASE (EC 2.5.1.15)
695	696	RXA00106	GR00014	17469	17924	DIHYDROFOLATE REDUCTASE (EC 1.5.1.3)
697	698	RXA00989	GR00280	2903	1371	FOLYLYPOLYGLUTAMATE SYNTHASE (EC 6.3.2.17)
699	700	RXA01517	GR00424	22752	23228	2-AMINO-4-HYDROXY-6-HYDROXYMETHYLDIHYDROPTERIDINE PYROPHOSPHOKINASE (EC 2.7.6.3)
701	702	RXA00579	GR00156	5946	4087	PARA-AMINOBENZOATE SYNTHASE COMPONENT I (EC 4.1.3.-)
703	704	RXA00958	GR00264	1130	1753	PARA-AMINOBENZOATE SYNTHASE GLUTAMINE AMIDOTRANSFERASE COMPONENT II (EC 4.1.3.-) / ANTHRANILATE SYNTHASE COMPONENT II (EC 4.1.3.27)
705	706	RXA02790	GR00777	5806	6948	4-AMINO-4-DEOXYCHORISMATE LYASE (EC 4.-.-.-)
707	708	RXA00106	GR00014	17469	17924	DIHYDROFOLATE REDUCTASE (EC 1.5.1.3)
709	710	RXN02198	WV0302	9228	11726	5-METHYLTETRAHYDROFOLATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.13)
711	712	F RXA02198	GR00646	2483	6	5-METHYLTETRAHYDROFOLATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.13)
713	714	RXN02085	WV0126	8483	10717	5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE METHYLTRANSFERASE
715	716	F RXA02085	GR00629	3496	5295	5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.14)
717	718	F RXA02086	GR00629	5252	5731	5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.14)
719	720	RXN02648				5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.14)
721	722	F RXA02648	GR00751	5254	4730	5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.14)
723	724	F RXA02658	GR00752	14764	15447	5-METHYLTETRAHYDROPTEROYLTRIGLUTAMATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.14)
725	726	RXS02197				5-METHYLTETRAHYDROFOLATE--HOMOCYSTEINE METHYLTRANSFERASE (EC 2.1.1.13)
727	728	RXC00988				PROTEIN INVOLVED IN FOLATE METABOLISM
729	730	RXC01518				MEMBRANE SPANNING PROTEIN INVOLVED IN FOLATE METABOLISM
731	732	RXC01942				ATP-BINDING PROTEIN INVOLVED IN FOLATE METABOLISM

Molybdopterin Metabolism

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
733	734	RXN02802	WV0112	17369	16299	MOLYBDOPTERIN BIOSYNTHESIS MOEB PROTEIN
735	736	F RXA02802	GR00783	7	474	MOLYBDOPTERIN BIOSYNTHESIS MOEB PROTEIN
737	738	F RXA00438	GR00103	362	796	MOLYBDOPTERIN BIOSYNTHESIS MOEB PROTEIN
739	740	RXN00437	WV0112	17824	17369	MOLYBDOPTERIN (MPT) CONVERTING FACTOR, SUBUNIT 2
741	742	F RXA00437	GR00103	3	362	MOLYBDOPTERIN (MPT) CONVERTING FACTOR, SUBUNIT 2
743	744	RXN00439	WV0112	18742	18275	MOLYBDOPTERIN CO-FACTOR SYNTHESIS PROTEIN
745	746	F RXA00439	GR00104	2	196	MOLYBDOPTERIN CO-FACTOR SYNTHESIS PROTEIN
747	748	F RXA00442	GR00105	830	1087	MOLYBDOPTERIN CO-FACTOR SYNTHESIS PROTEIN

Table 1 (continued)

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Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
813	814	RXN01162	VV0088	1849	524	PRECORRIN-6Y METHYLASE (EC 2.1.1.-)
815	816	F RXA01162	GR00330	1248	4	PRECORRIN-6Y METHYLASE (EC 2.1.1.-)
817	818	RXA01692	GR00474	1498	749	UROPORPHYRIN-III C-METHYLTRANSFERASE (EC 2.1.1.107)
819	820	RXN00371	VV0226	4180	5973	UROPORPHYRIN-III C-METHYLTRANSFERASE (EC 2.1.1.107) / UROPORPHYRIN-III SYNTHASE (EC 4.2.1.75)
821	822	F RXA00371	GR00078	929	6	UROPORPHYRIN-III C-METHYLTRANSFERASE (EC 2.1.1.107) / UROPORPHYRIN-III SYNTHASE (EC 4.2.1.75)
823	824	F RXA00374	GR00079	1102	371	UROPORPHYRIN-III C-METHYLTRANSFERASE (EC 2.1.1.107) / UROPORPHYRIN-III SYNTHASE (EC 4.2.1.75)
825	826	RXN00383	VV0223	4206	2863	PROTOPORPHYRIN-III C-METHYLTRANSFERASE (EC 1.3.3.4)
827	828	F RXA00376	GR00081	287	6	PROTOPORPHYRIN-III C-METHYLTRANSFERASE (EC 1.3.3.4)
829	830	F RXA00383	GR00082	3876	2863	PROTOPORPHYRIN-III C-METHYLTRANSFERASE (EC 1.3.3.4)
831	832	RXA01253	GR00365	2536	1787	PROTOPORPHYRIN-III C-METHYLTRANSFERASE (EC 1.3.3.4)
833	834	RXA02134	GR00639	1721	801	COBYRIC ACID SYNTHASE
835	836	RXA02135	GR00639	2809	1736	COBALAMIN (5'-PHOSPHATE) SYNTHASE
837	838	RXA02136	GR00639	3362	2841	NICOTINATE-NUCLEOTIDE-DIMETHYLBENZIMIDAZOLE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.21)
839	840	RXN03114	VV0088	1	552	COBINAMIDE KINASE / COBINAMIDE PHOSPHATE GUANYLYLTRANSFERASE
841	842	RXN01810	VV0082	1739	663	COBG PROTEIN (EC 1.-.-.-)
843	844	RXS03205				HEMIN-BINDING PERIPLASMIC PROTEIN HMUT PRECURSOR
845	846	F RXA00306				HEMK PROTEIN
847	848	RXC01715				HEMK PROTEIN CYTOSOLIC PROTEIN INVOLVED IN PORPHYRIN METABOLISM

Vitamin C precursors

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
849	850	RXN00420	VV0112	2511	1048	L-GULONOLACTONE OXIDASE (EC 1.1.3.8)
851	852	F RXA00420	GR00096	2	541	L-GULONOLACTONE OXIDASE (EC 1.1.3.8)
853	854	F RXA00426	GR00097	1737	2258	L-GULONOLACTONE OXIDASE (EC 1.1.3.8)
855	856	RXN00708	VV0005	4678	3872	2,5-DIKETO-D-GLUCONIC ACID REDUCTASE (EC 1.1.1.-)
857	858	F RXA00708	GR00185	2030	1359	2,5-DIKETO-D-GLUCONIC ACID REDUCTASE (EC 1.1.1.-)
859	860	RXA02373	GR00888	1540	626	2,5-DIKETO-D-GLUCONIC ACID REDUCTASE (EC 1.1.1.-) oxoglutarate semialdehyde dehydrogenase (EC 1.2.1.-)
861	862	RXS00389				ACETOACETYL-COA REDUCTASE (EC 1.1.1.36)
863	864	RXS00419				MEMBRANE SPANNING PROTEIN INVOLVED IN METABOLISM OF VITAMIN C PRECURSORS
865	866	RXC00416				OXIDOREDUCTASE INVOLVED IN METABOLISM OF VITAMIN C PRECURSORS
867	868	RXC02206				

Vitamin K2

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
869	870	RXS03074				S-ADENOSYLMETHIONINE:2-DEMETHYLMENAQUINONE METHYLTRANSFERASE (EC 2.1.-.-)

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
871	872	F RXA02906	GR10044	1142	645	S-ADENOSYLMETHIONINE:2-DEMETHYLMENAUINONE METHYLTRANSFERASE (EC 2.1.-.-)
873	874	RXA02315	GR00665	8011	6383	2-SUCCINYL-6-HYDROXY-2,4-CYCLOHEXADIENE-1-CARBOXYLATE SYNTHASE /2-OXOGLUTARATE DECARBOXYLASE (EC 4.1.1.71)
875	876	RXA02319	GR00665	9977	10933	NAPHTHOATE SYNTHASE (EC 4.1.3.36)
877	878	RXS00393				1,4-DIHYDROXY-2-NAPHTHOATE OCTAPRENYLTRANSFERASE (EC 2.5.-.-)
879	880	F RXA00393	GR00086	4030	4911	1,4-DIHYDROXY-2-NAPHTHOATE OCTAPRENYLTRANSFERASE (EC 2.5.-.-)
881	882	RXA00391	GR00086	2031	2750	O-SUCCINYLBENZOIC ACID-COA LIGASE (EC 6.2.1.26)
883	884	RXS02908				O-SUCCINYLBENZOIC ACID-COA LIGASE (EC 6.2.1.26)

Ubiquinone biosynthesis

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
885	886	RXA00997	GR00283	2389	1808	3-DEMETHYLBUBIQUINONE-9 3-METHYLTRANSFERASE (EC 2.1.1.64)
887	888	RXA02189	GR00642	986	249	3-DEMETHYLBUBIQUINONE-9 3-METHYLTRANSFERASE (EC 2.1.1.64)
889	890	RXA02311	GR00665	3073	2384	3-DEMETHYLBUBIQUINONE-9 3-METHYLTRANSFERASE (EC 2.1.1.64)
891	892	RXN02912	VV0135	13299	12547	UBIQUINONE/MENAUINONE BIOSYNTHESIS METHYLTRANSFERASE UBIE (EC 2.1.1.-)
893	894	RXS00998				COMA OPERON PROTEIN 2

Purines and Pyrimidines and other Nucleotides

Regulation of purine and pyrimidine biosynthesis pathways

Purine metabolism

Purine Biosynthesis

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
895	896	RXA01215	GR00352	1187	213	RIBOSE-PHOSPHATE PYROPHOSPHOKINASE, PRPP synthetase (EC 2.7.6.1)
897	898	RXN00558	VV0103	8235	9581	AMIDOPHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.14)
899	900	F RXA00558	GR00148	61	501	AMIDOPHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.14)
901	902	RXN00626	VV0135	11624	10362	PHOSPHORIBOSYLAMINE-GLYCINE LIGASE (EC 6.3.4.13)
903	904	F RXA00629	GR00165	1450	1713	PHOSPHORIBOSYLAMINE-GLYCINE LIGASE (EC 6.3.4.13)
905	906	F RXA00626	GR00164	1	780	PHOSPHORIBOSYLAMINE-GLYCINE LIGASE, GARS (EC 6.3.4.13)
907	908	RXA02623	GR00746	4875	4285	PHOSPHORIBOSYLAMINE-GLYCINE LIGASE (EC 6.3.4.13) / PHOSPHORIBOSYLFORMYLYLCINAMIDINE CYCLO-LIGASE (EC 6.3.3.1) / PHOSPHORIBOSYLGLYCINAMIDE FORMYLYLTRANSFERASE (EC 2.1.2.2)
909	910	RXA01442	GR00418	10277	9054	PHOSPHORIBOSYLGLYCINAMIDE FORMYLYLTRANSFERASE 2 (EC 2.1.2.-)

Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
911	912	RXN00537	VV0103	3351	5636	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE SYNTHASE (EC 6.3.5.3)
913	914	F RXA02805	GR00786	54	638	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE SYNTHASE (EC 6.3.5.3)
915	916	F RXA00537	GR00138	23	697	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE SYNTHASE (EC 6.3.5.3)
917	918	F RXA00561	GR00150	2	280	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE SYNTHASE (EC 6.3.5.3)
919	920	RXA00541	GR00139	2269	2937	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE SYNTHASE (EC 6.3.5.3)
921	922	RXA00620	GR00163	3049	3939	PHOSPHORIBOSYLAMIDIMIDAZOLE-SUCCINOCARBOXAMIDE SYNTHASE (EC 6.3.2.6)
923	924	RXN00770	VV0103	9614	10783	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE CYCLO-LIGASE (EC 6.3.3.1)
925	926	F RXA00557	GR00147	15	818	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE CYCLO-LIGASE (EC 6.3.3.1)
927	928	F RXA00770	GR00204	7809	7495	PHOSPHORIBOSYLFORMYLGLYCINAMIDINE CYCLO-LIGASE (EC 6.3.3.1)
929	930	RXN02345	VV0078	4788	5984	PHOSPHORIBOSYLAMINOIMIDAZOLE CARBOXYLASE ATPASE SUBUNIT (EC 4.1.1.21)
931	932	F RXA02345	GR00676	1534	725	PHOSPHORIBOSYLAMINOIMIDAZOLE CARBOXYLASE ATPASE SUBUNIT (EC 4.1.1.21)
933	934	RXN02350	VV0078	8369	8863	PHOSPHORIBOSYLAMINOIMIDAZOLE CARBOXYLASE CATALYTIC SUBUNIT (EC 4.1.1.21)
935	936	F RXA02346	GR00677	127	5	PHOSPHORIBOSYLAMINOIMIDAZOLE CARBOXYLASE CATALYTIC SUBUNIT (EC 4.1.1.21)
937	938	F RXA02350	GR00678	1120	911	PHOSPHORIBOSYLAMINOIMIDAZOLE CARBOXYLASE CATALYTIC SUBUNIT (EC 4.1.1.21)
939	940	RXA01087	GR00304	498	1373	PHOSPHORIBOSYLAMINOIMIDAZOLE CARBOXYLASE (EC 4.1.1.21)
941	942	RXA00619	GR00163	793	2220	ADENYLOSUCCINATE LYASE (EC 4.3.2.2)
943	944	RXA02622	GR00746	4274	2715	PHOSPHORIBOSYLAMINOIMIDAZOLE CARBOXYLASE FORMYLTRANSFERASE (EC 2.1.2.3) / IMP CYCLOHYDROLASE (EC 3.5.4.10)
945	946	RXN00488	VV0086	19066	20583	INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE (EC 1.1.1.205)
947	948	F RXA00492	GR00122	1171	1644	INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE (EC 1.1.1.205)
949	950	F RXA00488	GR00121	1	534	INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE (EC 1.1.1.205)
951	952	RXA02469	GR00715	1927	497	INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE (EC 1.1.1.205)
953	954	RXN00487	VV0086	23734	25302	GMP SYNTHASE [GLUTAMINE-HYDROLYZING] (EC 6.3.5.2)
955	956	F RXA00487	GR00120	712	2097	GMP SYNTHASE (EC 6.3.4.1)
957	958	RXA02237	GR00654	4577	5146	GUANYLATE KINASE (EC 2.7.4.8)
959	960	RXA01446	GR00418	17765	16476	ADENYLOSUCCINATE SYNTHETASE (EC 6.3.4.4)
961	962	RXA00619	GR00163	793	2220	ADENYLOSUCCINATE LYASE (EC 4.3.2.2)
963	964	RXA00688	GR00179	10443	10985	ADENYLATE KINASE (EC 2.7.4.3)
965	966	RXA00266	GR00040	3769	3362	NUCLEOSIDE DIPHOSPHATE KINASE (EC 2.7.4.6)

GMP, GDP, AMP and ADP synthesis, from inosine-5'-monophosphate (IMP)

Table 1 (continued)

GMP/AMP degrading activities

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
967	968	RXA00489	GR00121	654	1775	GMP REDUCTASE (EC 1.6.6.8)
969	970	RXN02281	VV0152	1893	3323	AMP NUCLEOSIDASE (EC 3.2.2.4)
971	972	F RXA02281	GR00659	1101	34	AMP NUCLEOSIDASE (EC 3.2.2.4)

Pyrimidine metabolism**Pyrimidine biosynthesis de novo:**

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
973	974	RXA00147	GR00022	9722	10900	CARBAMOYL-PHOSPHATE SYNTHASE SMALL CHAIN (EC 6.3.5.5)
975	976	RXA00145	GR00022	7258	8193	ASPARTATE CARBAMOYLTRANSFERASE CATALYTIC CHAIN (EC 2.1.3.2)
977	978	RXA00146	GR00022	8249	9589	DIHYDROOROTASE (EC 3.5.2.3)
979	980	RXA02208	GR00647	2	1003	DIHYDROOROTATE DEHYDROGENASE (EC 1.3.3.1)
981	982	RXA01660	GR00462	591	1142	OROTATE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.10)
983	984	RXA02235	GR00654	3207	4040	OROTIDINE 5-PHOSPHATE DECARBOXYLASE (EC 4.1.1.23)
985	986	RXN01892	VV0150	3020	3748	URIDYLATE KINASE (EC 2.7.4.-)
987	988	F RXA01892	GR00542	47	775	URIDYLATE KINASE (EC 2.7.4.-)
989	990	RXA00105	GR00014	16672	17346	THYMIDYLATE SYNTHASE (EC 2.1.1.45)
991	992	RXA00131	GR00020	7621	7013	THYMIDYLATE KINASE (EC 2.7.4.9)
993	994	RXA00266	GR00040	3769	3362	NUCLEOSIDE DIPHOSPHATE KINASE (EC 2.7.4.6)
995	996	RXA00718	GR00188	4576	5283	CYTIDYLATE KINASE (EC 2.7.4.14)
997	998	RXA01599	GR00447	8780	10441	CTP SYNTHASE (EC 6.3.4.2)
999	1000	RXN02234	VV0134	24708	28046	CARBAMOYL-PHOSPHATE SYNTHASE LARGE CHAIN (EC 6.3.5.5)
1001	1002	F RXA02234	GR00654	1	3198	CARBAMOYL-PHOSPHATE SYNTHASE LARGE CHAIN (EC 6.3.5.5)
1003	1004	RXN00450	VV0112	34491	34814	CYTOSINE DEAMINASE (EC 3.5.4.1)
1005	1006	F RXA00450	GR00110	322	5	CYTOSINE DEAMINASE (EC 3.5.4.1)
1007	1008	RXN02272	VV0020	15566	16810	CYTOSINE DEAMINASE (EC 3.5.4.1)
1009	1010	F RXA02272	GR00655	6691	7935	CREATININE DEAMINASE (EC 3.5.4.21)
1011	1012	RXN03004	VV0237	1862	2341	DEOXYCYTIDINE TRIPHOSPHATE DEAMINASE (EC 3.5.4.13)
1013	1014	RXN03137	VV0129	9680	9579	THYMIDYLATE SYNTHASE (EC 2.1.1.45)
1015	1016	RXN03171	VV0328	568	1080	URACIL PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.9)
1017	1018	F RXA02857	GR10003	570	1082	URACIL PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.9)

Table 1 (continued)
Purine and pyrimidine base, nucleoside and nucleotide salvage, interconversion, reduction and degradation:
Purines:

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
1019	1020	RXA02771	GR00772	1329	1883	ADENINE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.7)
1021	1022	RXA01512	GR00424	17633	18232	HYPOXANTHINE-GUANINE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.8)
1023	1024	RXA02031	GR00618	3820	3347	XANTHINE-GUANINE PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.22)
1025	1026	RXA00981	GR00276	3388	4017	GTP PYROPHOSPHOKINASE (EC 2.7.6.5)
1027	1028	RXN02772	VW0171	2045	1011	GUANOSINE-3',5'-BIS(DIPHOSPHATE) 3'-PYROPHOSPHOHYDROLASE (EC 3.1.7.2)
1029	1030	F RXA02772	GR00772	1962	2741	GUANOSINE-3',5'-BIS(DIPHOSPHATE) 3'-PYROPHOSPHOHYDROLASE (EC 3.1.7.2)
1031	1032	F RXA02773	GR00772	2741	2902	GUANOSINE-3',5'-BIS(DIPHOSPHATE) 3'-PYROPHOSPHOHYDROLASE (EC 3.1.7.2)
1033	1034	RXA01835	GR00517	3147	3677	GUANOSINE-3',5'-BIS(DIPHOSPHATE) 3'-PYROPHOSPHOHYDROLASE (EC 3.1.7.2)
1035	1036	RXA01483	GR00422	19511	18240	DEOXYGUANOSINETRIPHOSPHATE TRIPHOSPHOHYDROLASE (EC 3.1.5.1)
1037	1038	RXN01027	VW0143	5761	6768	DIADENOSINE 5',5''-P ₁ ,P ₄ -TETRAPHOSPHATE HYDROLASE (EC 3.6.1.17)
1039	1040	F RXA01024	GR00293	661	5	DIADENOSINE 5',5''-P ₁ ,P ₄ -TETRAPHOSPHATE HYDROLASE (EC 3.6.1.17)
1041	1042	F RXA01027	GR00294	2580	2347	DIADENOSINE 5',5''-P ₁ ,P ₄ -TETRAPHOSPHATE HYDROLASE (EC 3.6.1.17)
1043	1044	RXA01528	GR00425	5653	5126	DIADENOSINE 5',5''-P ₁ ,P ₄ -TETRAPHOSPHATE HYDROLASE (EC 3.6.1.17)
1045	1046	RXA00072	GR00012	446	6	PHOSPHOADENOSINE PHOSPHOSULFATE REDUCTASE (EC 1.8.99.4)
1047	1048	RXA01878	GR00537	1239	2117	DIMETHYLADENOSINE TRANSFERASE (EC 2.1.1.-)
1049	1050	RXN02281	VW0152	1893	3323	AMP NUCLEOSIDASE (EC 3.2.2.4)
1051	1052	F RXA02281	GR00659	1101	34	AMP NUCLEOSIDASE (EC 3.2.2.4)
1053	1054	RXN01240	VW0090	30442	29420	GTP PYROPHOSPHOKINASE (EC 2.7.6.5)
1055	1056	RXN02008	VW0171	1138	5	GUANOSINE-3',5'-BIS(DIPHOSPHATE) 3'-PYROPHOSPHOHYDROLASE (EC 3.1.7.2)

Pyrimidine and purine metabolism:

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
1057	1058	RXN01940	VW0120	10268	9333	INOSINE-URIDINE PREFERRING NUCLEOSIDE HYDROLASE (EC 3.2.2.1)
1059	1060	F RXA01940	GR00557	3	581	INOSINE-URIDINE PREFERRING NUCLEOSIDE HYDROLASE (EC 3.2.2.1)
1061	1062	RXA02559	GR00731	5418	6320	INOSINE-URIDINE PREFERRING NUCLEOSIDE HYDROLASE (EC 3.2.2.1)
1063	1064	RXA02497	GR00720	10059	10985	EXOPOLYPHOSPHATASE (EC 3.6.1.11)
1065	1066	RXN01079	VW0084	38084	35982	RIBONUCLEOSIDE-DIPHOSPHATE REDUCTASE ALPHA CHAIN (EC 1.17.4.1)
1067	1068	F RXA01079	GR00301	693	4	RIBONUCLEOSIDE-DIPHOSPHATE REDUCTASE ALPHA CHAIN (EC 1.17.4.1)
1069	1070	F RXA01084	GR00302	3402	2062	RIBONUCLEOSIDE-DIPHOSPHATE REDUCTASE ALPHA CHAIN (EC 1.17.4.1)
1071	1072	RXN01920	VW0084	32843	31842	RIBONUCLEOSIDE-DIPHOSPHATE REDUCTASE ALPHA CHAIN (EC 1.17.4.1)
1073	1074	F RXA01920	GR00550	1321	908	RIBONUCLEOTIDE REDUCTASE SUBUNIT R2F
1075	1076	RXA01080	GR00301	1240	797	NRD1 PROTEIN
1077	1078	RXA00867	GR00237	1	627	POLYRIBONUCLEOTIDE NUCLEOTIDYLTRANSFERASE (EC 2.7.7.8)
1079	1080	RXA01416	GR00413	2	631	POLYRIBONUCLEOTIDE NUCLEOTIDYLTRANSFERASE (EC 2.7.7.8)
1081	1082	RXA01486	GR00423	660	4	POLYRIBONUCLEOTIDE NUCLEOTIDYLTRANSFERASE (EC 2.7.7.8)

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Table 1 (continued)

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
1083	1084	RXA01678	GR00467	7162	7689	2'-3'-CYCLIC-NUCLEOTIDE 2'-PHOSPHODIESTERASE (EC 3.1.4.16)
1085	1086	RXA01679	GR00467	7729	8964	2'-3'-CYCLIC-NUCLEOTIDE 2'-PHOSPHODIESTERASE (EC 3.1.4.16)
1087	1088	RXN01488	VW0139	39842	40789	INOSINE-URIDINE PREFERRING NUCLEOSIDE HYDROLASE (EC 3.2.2.1)
1089	1090	RXC00540				CYTOSOLIC PROTEIN INVOLVED IN PURINE METABOLISM
1091	1092	RXC00560				PROTEIN INVOLVED IN PURINE METABOLISM
1093	1094	RXC01088				CYTOSOLIC PROTEIN INVOLVED IN PURINE METABOLISM
1095	1096	RXC02624				MEMBRANE SPANNING PROTEIN INVOLVED IN PURINE METABOLISM
1097	1098	RXC02665				PROTEIN INVOLVED IN PURINE METABOLISM
1099	1100	RXC02770				LIPOPROTEIN INVOLVED IN PURINE METABOLISM
1101	1102	RXC02238				PROTEIN INVOLVED IN METABOLISM OF S-ADENOSYLMETHIONINE, PURINES AND PANTOTHENATE
1103	1104	RXC01946				ABC TRANSPORTER ATP-BINDING PROTEIN INVOLVED IN PURINE METABOLISM

Pyrimidines:

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig	NT Start	NT Stop	Function
1105	1106	RXN03171	VW0328	568	1080	URACIL PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.9)
1107	1108	F RXA02857	GR10003	570	1082	URACIL PHOSPHORIBOSYLTRANSFERASE (EC 2.4.2.9)
1109	1110	RXN00450	VW0112	34491	34814	CYTOSINE DEAMINASE (EC 3.5.4.1)
1111	1112	F RXA00450	GR00110	322	5	CYTOSINE DEAMINASE (EC 3.5.4.1)
1113	1114	RXA00465	GR00117	337	828	CYTOSINE DEAMINASE (EC 3.5.4.1)
1115	1116	RXA00717	GR00188	3617	4576	RIBOSOMAL LARGE SUBUNIT PSEUDOURIDINE SYNTHASE B (EC 4.2.1.70)
1117	1118	RXA01894	GR00542	1622	2476	PHOSPHATIDATE CYTIDYLTRANSFERASE (EC 2.7.7.41)
1119	1120	RXA02536	GR00726	8581	7826	BETA-UREIDOPROPIONASE (EC 3.5.1.6)
1121	1122	RXN01209	VW0270	1019	2446	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
1123	1124	F RXA01209	GR00348	1019	2446	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
1125	1126	RXN01617	VW0050	22187	22858	PHOSPHOMETHYLPYRIMIDINE KINASE (EC 2.7.4.7)
1127	1128	F RXA01617	GR00451	2	616	CYTOSOLIC PROTEIN INVOLVED IN PYRIMIDINE METABOLISM
1129	1130	RXC01600				CYTOSOLIC PROTEIN INVOLVED IN PYRIMIDINE METABOLISM
1131	1132	RXC01622				EXPORTED PROTEIN INVOLVED IN METABOLISM OF PYRIDINES AND ADENOSYLMOCYSTEINE
1133	1134	RXC00128				CYTOSOLIC PROTEIN INVOLVED IN PYRIMIDINE METABOLISM
1135	1136	RXC01709				EXPORTED PROTEIN INVOLVED IN PYRIMIDINE METABOLISM
1137	1138	RXC02207				

Table 1 (continued)**Sugars****Trehalose**

Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO	Identification Code	Contig.	NT Start	NT Stop	Function
1139	1140	RXA00347	GR00065	246	1013	TREHALOSE-PHOSPHATASE (EC 3.1.3.12)
1141	1142	RXN01239	VV0090	32921	30489	maltooligosyltrehalose synthase
1143	1144	F RXA01239	GR00358	5147	7579	maltooligosyltrehalose synthase
1145	1146	RXA02645	GR00751	714	2543	maltooligosyltrehalose trehalohydrolase
1147	1148	RXN02355	VV0051	735	4	TREHALOSE/MALTOSE BINDING PROTEIN
1149	1150	RXN02909	VV0135	38532	39017	Hypothetical Trehalose-Binding Protein
1151	1152	RXS00349				Hypothetical Trehalose Transport Protein
1153	1154	RXS03183				TREHALOSE/MALTOSE BINDING PROTEIN
1155	1156	RXC00874				TRANSMEMBRANE PROTEIN INVOLVED IN TREHALOSE METABOLISM

TABLE 2 - Excluded Genes

GenBank™ Accession No.	Gene Name	Gene Function	Reference
A09073	ppg	Phosphoenol pyruvate carboxylase	Bachmann, B. et al. "DNA fragment coding for phosphoenolpyruvate carboxylase, recombinant DNA carrying said fragment, strains carrying the recombinant DNA and method for producing L-aminino acids using said strains," Patent: EP 0358940-A 3 03/21/90
A45579, A45581, A45583, A45585 A45587		Threonine dehydratase	Moeckel, B. et al. "Production of L-isoleucine by means of recombinant micro-organisms with deregulated threonine dehydratase," Patent: WO 9519442-A 5 07/20/95
AB003132	murC; ftsQ; ftsZ		Kobayashi, M. et al. "Cloning, sequencing, and characterization of the ftsZ gene from coryneform bacteria," <i>Biochem. Biophys. Res. Commun.</i> , 236(2):383-388 (1997)
AB015023	murC; ftsQ		Wachi, M. et al. "A murC gene from Coryneform bacteria," <i>Appl. Microbiol. Biotechnol.</i> , 51(2):223-228 (1999)
AB018530	disR		Kimura, E. et al. "Molecular cloning of a novel gene, disR, which rescues the detergent sensitivity of a mutant derived from <i>Brevibacterium lactofermentum</i> ," <i>Biosci. Biotechnol. Biochem.</i> , 60(10):1565-1570 (1996)
AB018531	disR1; disR2		
AB020624	murI	D-glutamate racemase	
AB023377	tkl	transketolase	
AB024708	glbB; gltD	Glutamine 2-oxoglutarate aminotransferase large and small subunits	
AB025424	acn	aconitase	
AB027714	rep	Replication protein	
AB027715	rep; aad	Replication protein; aminoglycoside adenylyltransferase	
AF005242	argC	N-acetylglutamate-5-semialdehyde dehydrogenase	
AF005635	glnA	Glutamine synthetase	
AF030405	hisF	cyclase	
AF030520	argG	Argininosuccinate synthetase	
AF031518	argF	Ornithine carbamoyltransferase	
AF036932	aroD	3-dehydroquinate dehydratase	
AF038548	pyc	Pyruvate carboxylase	

Table 2 (continued)

	Promoter and operator regions of tryptophan operon	
E01377		Matsui, K. et al. "Tryptophan operon, peptide and protein coded thereby, utilization of tryptophan operon gene expression and production of tryptophan," Patent: JP 1987244382-A 1 10/24/87
E03937	Biotin-synthase	Hatakeyama, K. et al. "DNA fragment containing gene capable of coding biotin synthetase and its utilization," Patent: JP 1992278088-A 1 10/02/92
E04040	Diamino pelargonic acid aminotransferase	Kohama, K. et al. "Gene coding diaminopelargonic acid aminotransferase and deshiobiotin synthetase and its utilization," Patent: JP 1992330284-A 1 11/18/92
E04041	Deshiobiotinsynthetase	Kohama, K. et al. "Gene coding diaminopelargonic acid aminotransferase and deshiobiotin synthetase and its utilization," Patent: JP 1992330284-A 1 11/18/92
E04307	Flavum aspartase	Kurusu, Y. et al. "Gene DNA coding aspartase and utilization thereof," Patent: JP 1993030977-A 1 02/09/93
E04376	Isocitric acid lyase	Katsumata, R. et al. "Gene manifestation controlling DNA," Patent: JP 1993056782-A 3 03/09/93
E04377	Isocitric acid lyase N-terminal fragment	Katsumata, R. et al. "Gene manifestation controlling DNA," Patent: JP 1993056782-A 3 03/09/93
E04484	Prephenate dehydratase	Sotouchi, N. et al. "Production of L-phenylalanine by fermentation," Patent: JP 1993076352-A 2 03/30/93
E05108	Aspartokinase	Fugono, N. et al. "Gene DNA coding Aspartokinase and its use," Patent: JP 1993184366-A 1 07/27/93
E05112	Dihydro-dipichorinate synthetase	Hatakeyama, K. et al. "Gene DNA coding dihydrodipicolinic acid synthetase and its use," Patent: JP 1993184371-A 1 07/27/93
E05776	Diaminopimelic acid dehydrogenase	Kobayashi, M. et al. "Gene DNA coding Diaminopimelic acid dehydrogenase and its use," Patent: JP 1993284970-A 1 11/02/93
E05779	Threonine synthase	Kohama, K. et al. "Gene DNA coding threonine synthase and its use," Patent: JP 1993284972-A 1 11/02/93
E06110	Prephenate dehydratase	Kikuchi, T. et al. "Production of L-phenylalanine by fermentation method," Patent: JP 1993344881-A 1 12/27/93
E06111	Mutated Prephenate dehydratase	Kikuchi, T. et al. "Production of L-phenylalanine by fermentation method," Patent: JP 1993344881-A 1 12/27/93
E06146	Acetohydroxy acid synthetase	Inui, M. et al. "Gene capable of coding Acetohydroxy acid synthetase and its use," Patent: JP 1993344893-A 1 12/27/93
E06825	Aspartokinase	Sugimoto, M. et al. "Mutant aspartokinase gene," patent: JP 1994062866-A 1 03/08/94
E06826	Mutated aspartokinase alpha subunit	Sugimoto, M. et al. "Mutant aspartokinase gene," patent: JP 1994062866-A 1 03/08/94

Table 2 (continued)

E06827		Mutated aspartokinase alpha subunit	Sugimoto, M. et al. "Mutant aspartokinase gene," patent: JP 1994062866-A 1 03/08/94
E07701	secY		Honno, N. et al. "Gene DNA participating in integration of membrane protein to membrane," Patent: JP 1994169780-A 1 06/21/94
E08177		Aspartokinase	Sato, Y. et al. "Genetic DNA capable of coding Aspartokinase released from feedback inhibition and its utilization," Patent: JP 1994261766-A 1 09/20/94
E08178, E08179, E08180, E08181, E08182		Feedback inhibition-released Aspartokinase	Sato, Y. et al. "Genetic DNA capable of coding Aspartokinase released from feedback inhibition and its utilization," Patent: JP 1994261766-A 1 09/20/94
E08232		Acetohydroxy-acid isomeroreductase	Inui, M. et al. "Gene DNA coding acetohydroxy acid isomeroreductase," Patent: JP 1994277067-A 1 10/04/94
E08234	secE		Asai, Y. et al. "Gene DNA coding for translocation machinery of protein," Patent: JP 1994277073-A 1 10/04/94
E08643		FT aminotransferase and desthiobiotin synthetase promoter region	Hatakeyama, K. et al. "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031476-A 1 02/03/95
E08646		Biotin synthetase	Hatakeyama, K. et al. "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031476-A 1 02/03/95
E08649		Aspartase	Kohama, K. et al. "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031478-A 1 02/03/95
E08900		Dihydrodipicolinate reductase	Madori, M. et al. "DNA fragment containing gene coding Dihydrodipicolinate acid reductase and utilization thereof," Patent: JP 1995075578-A 1 03/20/95
E08901		Diaminopimelic acid decarboxylase	Madori, M. et al. "DNA fragment containing gene coding Diaminopimelic acid decarboxylase and utilization thereof," Patent: JP 1995075579-A 1 03/20/95
E12594		Serine hydroxymethyltransferase	Hatakeyama, K. et al. "Production of L-tryptophan," Patent: JP 1997028391-A 1 02/04/97
E12760, E12759, E12758		transposase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12764		Arginyl-tRNA synthetase; diaminopimelic acid decarboxylase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12767		Dihydrodipicolinic acid synthetase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12770		aspartokinase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12773		Dihydrodipicolinic acid reductase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97

Table 2 (continued)

E13655		Glucose-6-phosphate dehydrogenase	Hatakeyama, K. et al. "Glucose-6-phosphate dehydrogenase and DNA capable of coding the same," Patent: JP 1997224661-A 1 09/02/97
L01508	ilvA	Threonine dehydratase	Moeckel, B. et al. "Functional and structural analysis of the threonine dehydratase of <i>Corynebacterium glutamicum</i> ," <i>J. Bacteriol.</i> , 174:8065-8072 (1992)
L07603	EC 4.2.1.15	3-deoxy-D-arabinoheptulosonate-7-phosphate synthase	Chen, C. et al. "The cloning and nucleotide sequence of <i>Corynebacterium glutamicum</i> 3-deoxy-D-arabinoheptulosonate-7-phosphate synthase gene," <i>FEMS Microbiol. Lett.</i> , 107:223-230 (1993)
L09232	ilvB; ilvN; ilvC	Acetohydroxy acid synthase large subunit; Acetohydroxy acid synthase small subunit; Acetohydroxy acid isomeroreductase	Keilhauer, C. et al. "Isoleucine synthesis in <i>Corynebacterium glutamicum</i> : molecular analysis of the ilvB-ilvN-ilvC operon," <i>J. Bacteriol.</i> , 175(17):5595-5603 (1993)
L18874	PtsM	Phosphoenolpyruvate sugar phosphotransferase	Fouet, A. et al. "Bacillus subtilis sucrose-specific enzyme II of the phosphotransferase system: expression in <i>Escherichia coli</i> and homology to enzymes II from enteric bacteria," <i>PNAS USA</i> , 84(24):8773-8777 (1987); Lee, J.K. et al. "Nucleotide sequence of the gene encoding the <i>Corynebacterium glutamicum</i> mannose enzyme II and analyses of the deduced protein sequence," <i>FEMS Microbiol. Lett.</i> , 119(1-2):137-145 (1994)
L27123	aceB	Malate synthase	Lee, H.-S. et al. "Molecular characterization of aceB, a gene encoding malate synthase in <i>Corynebacterium glutamicum</i> ," <i>J. Microbiol. Biotechnol.</i> , 4(4):256-263 (1994)
L27126		Pyruvate kinase	Jeiten, M. S. et al. "Structural and functional analysis of pyruvate kinase from <i>Corynebacterium glutamicum</i> ," <i>Appl. Environ. Microbiol.</i> , 60(7):2501-2507 (1994)
L28760	aceA	Isocitrate lyase	
L35906	dxr	Diphtheria toxin repressor	Oguiza, J.A. et al. "Molecular cloning, DNA sequence analysis, and characterization of the <i>Corynebacterium diphtheriae</i> dxrR from <i>Brevibacterium lactofermentum</i> ," <i>J. Bacteriol.</i> , 177(2):465-467 (1995)
M13774		Prephenate dehydratase	Follettie, M.T. et al. "Molecular cloning and nucleotide sequence of the <i>Corynebacterium glutamicum</i> pheA gene," <i>J. Bacteriol.</i> , 167:695-702 (1986)
M16175	5S rRNA		Park, Y.-H. et al. "Phylogenetic analysis of the coryneform bacteria by 5S rRNA sequences," <i>J. Bacteriol.</i> , 169:1801-1806 (1987)
M16663	trpE	Anthranilate synthase, 5' end	Sano, K. et al. "Structure and function of the trp operon control regions of <i>Brevibacterium lactofermentum</i> , a glutamic-acid-producing bacterium," <i>Gene</i> , 52:191-200 (1987)
M16664	trpA	Tryptophan synthase, 3' end	Sano, K. et al. "Structure and function of the trp operon control regions of <i>Brevibacterium lactofermentum</i> , a glutamic-acid-producing bacterium," <i>Gene</i> , 52:191-200 (1987)

Table 2 (continued)

		Phosphoenolpyruvate carboxylase	
M25819			O'Regan, M. et al. "Cloning and nucleotide sequence of the Phosphoenolpyruvate carboxylase-coding gene of <i>Corynebacterium glutamicum</i> ATCC13032," <i>Gene</i> , 77(2):237-251 (1989)
M85106		23S rRNA gene insertion sequence	Roller, C. et al. "Gram-positive bacteria with a high DNA G+C content are characterized by a common insertion within their 23S rRNA genes," <i>J. Gen. Microbiol.</i> , 138:1167-1175 (1992)
M85107, M85108		23S rRNA gene insertion sequence	Roller, C. et al. "Gram-positive bacteria with a high DNA G+C content are characterized by a common insertion within their 23S rRNA genes," <i>J. Gen. Microbiol.</i> , 138:1167-1175 (1992)
M89931	aecD; bmQ; yhbW	Beta C-S lyase; branched-chain amino acid uptake carrier; hypothetical protein yhbW	Rosol, I. et al. "The <i>Corynebacterium glutamicum</i> aecD gene encodes a C-S lyase with alpha, beta-elimination activity that degrades aminothyleysteine," <i>J. Bacteriol.</i> , 174(9):2968-2977 (1992); Tauch, A. et al. "Isoleucine uptake in <i>Corynebacterium glutamicum</i> ATCC 13032 is directed by the bmQ gene product," <i>Arch. Microbiol.</i> , 169(4):303-312 (1998)
S59299	trp	Leader gene (promoter)	Herry, D.M. et al. "Cloning of the trp gene cluster from a tryptophan-producing strain of <i>Corynebacterium glutamicum</i> : identification of a mutation in the trp leader sequence," <i>Appl. Environ. Microbiol.</i> , 59(3):791-799 (1993)
U11545	trpD	Anthraniolate phosphoribosyltransferase	O'Gara, J.P. and Dunican, L.K. (1994) Complete nucleotide sequence of the <i>Corynebacterium glutamicum</i> ATCC 21850 trpD gene." Thesis, Microbiology Department, University College Galway, Ireland.
U13922	cgIIIM; cgIIR; cglIIR	Putative type II 5-cytosine methyltransferase; putative type II restriction endonuclease; putative type I or type III restriction endonuclease	Schafer, A. et al. "Cloning and characterization of a DNA region encoding a stress-sensitive restriction system from <i>Corynebacterium glutamicum</i> ATCC 13032 and analysis of its role in intergeneric conjugation with <i>Escherichia coli</i> ," <i>J. Bacteriol.</i> , 176(23):7309-7319 (1994); Schafer, A. et al. "The <i>Corynebacterium glutamicum</i> cglIM gene encoding a 5-cytosine in an McrBC-deficient <i>Escherichia coli</i> strain," <i>Gene</i> , 203(2):95-101 (1997)
U14965	recA		
U31224	ppx		Ankri, S. et al. "Mutations in the <i>Corynebacterium glutamicum</i> proline biosynthetic pathway: A natural bypass of the proA step," <i>J. Bacteriol.</i> , 178(15):4412-4419 (1996)
U31225	proC	L-proline: NADP+ 5-oxido-reductase	Ankri, S. et al. "Mutations in the <i>Corynebacterium glutamicum</i> proline biosynthetic pathway: A natural bypass of the proA step," <i>J. Bacteriol.</i> , 178(15):4412-4419 (1996)
U31230	obg; proB; unkdh	?; gamma glutamyl kinase; similar to D-isomer specific 2-hydroxyacid dehydrogenases	Ankri, S. et al. "Mutations in the <i>Corynebacterium glutamicum</i> proline biosynthetic pathway: A natural bypass of the proA step," <i>J. Bacteriol.</i> , 178(15):4412-4419 (1996)

Table 2 (continued)

	bioB	Biotin synthase	
U31281			Serebriiskii, I.G., "Two new members of the bio B superfamily: Cloning, sequencing and expression of bio B genes of <i>Methylobacillus flagellatum</i> and <i>Corynebacterium glutamicum</i> ," <i>Gene</i> , 175:15-22 (1996)
U35023	thtR; accBC	Thiosulfate sulfurtransferase; acyl CoA carboxylase	Jager, W. et al. "A <i>Corynebacterium glutamicum</i> gene encoding a two-domain protein similar to biotin carboxylases and biotin-carboxyl-carrier proteins," <i>Arch. Microbiol.</i> , 166(2):76-82 (1996)
U43535	cmr	Multidrug resistance protein	Jager, W. et al. "A <i>Corynebacterium glutamicum</i> gene conferring multidrug resistance in the heterologous host <i>Escherichia coli</i> ," <i>J. Bacteriol.</i> , 179(7):2449-2451 (1997)
U43536	clpB	Heat shock ATP-binding protein	
U53587	aphA-3	3'5'-aminoglycoside phosphotransferase	
U89648		<i>Corynebacterium glutamicum</i> unidentified sequence involved in histidine biosynthesis, partial sequence	
X04960	trpA; trpB; trpC; trpD; trpE; trpG; trpL	Tryptophan operon	Matsui, K. et al. "Complete nucleotide and deduced amino acid sequences of the <i>Brevibacterium lactofermentum</i> tryptophan operon," <i>Nucleic Acids Res.</i> , 14(24):10113-10114 (1986)
X07563	lys A	DAP decarboxylase (meso-diaminopimelate decarboxylase, EC 4.1.1.20)	Yeh, P. et al. "Nucleic sequence of the lysA gene of <i>Corynebacterium glutamicum</i> and possible mechanisms for modulation of its expression," <i>Mol. Gen. Genet.</i> , 212(1):112-119 (1988)
X14234	EC 4.1.1.31	Phosphoenolpyruvate carboxylase	Eikmanns, B.J. et al. "The Phosphoenolpyruvate carboxylase gene of <i>Corynebacterium glutamicum</i> : Molecular cloning, nucleotide sequence, and expression," <i>Mol. Gen. Genet.</i> , 218(2):330-339 (1989); Lepiniec, L. et al. "Sorghum Phosphoenolpyruvate carboxylase gene family: structure, function and molecular evolution," <i>Plant. Mol. Biol.</i> , 21 (3):487-502 (1993)
X17313	fda	Fructose-bisphosphate aldolase	Von der Osten, C.H. et al. "Molecular cloning, nucleotide sequence and fine-structural analysis of the <i>Corynebacterium glutamicum</i> fda gene: structural comparison of C. glutamicum fructose-1, 6-biphosphate aldolase to class I and class II aldolases," <i>Mol. Microbiol.</i>
X53993	dapA	L-2, 3-dihydrodipicolinate synthetase (EC 4.2.1.52)	Bonnassie, S. et al. "Nucleic sequence of the dapA gene from <i>Corynebacterium glutamicum</i> ," <i>Nucleic Acids Res.</i> , 18(21):6421 (1990)
X54223		AttB-related site	Cianciotto, N. et al. "DNA sequence homology between att B-related sites of <i>Corynebacterium diphtheriae</i> , <i>Corynebacterium ulcerans</i> , <i>Corynebacterium glutamicum</i> , and the attP site of <i>lambdacorynephage</i> ," <i>FEMS. Microbiol. Lett.</i> , 66:299-302 (1990)
X54740	argS; lysA	Arginyl-tRNA synthetase; Diaminopimelate decarboxylase	Marcel, T. et al. "Nucleotide sequence and organization of the upstream region of the <i>Corynebacterium glutamicum</i> lysA gene," <i>Mol. Microbiol.</i> , 4(11):1819-1830 (1990)

Table 2 (continued)

X55994	trpL; trpE	Putative leader peptide; anthranilate synthase component 1	Heery, D.M. et al. "Nucleotide sequence of the <i>Corynebacterium glutamicum</i> trpE gene," <i>Nucleic Acids Res.</i> , 18(23):7138 (1990)
X56037	thrC	Threonine synthase	Han, K.S. et al. "The molecular structure of the <i>Corynebacterium glutamicum</i> threonine synthase gene," <i>Mol. Microbiol.</i> , 4(10):1693-1702 (1990)
X56075	attB-related site	Attachment site	Cianciotto, N. et al. "DNA sequence homology between att B-related sites of <i>Corynebacterium diphtheriae</i> , <i>Corynebacterium ulcerans</i> , <i>Corynebacterium glutamicum</i> , and the attP site of <i>lambdacorynephage</i> ," <i>FEMS. Microbiol. Lett.</i> , 66:299-302 (1990)
X57226	lysC-alpha; lysC-beta; asd	Aspartokinase-alpha subunit; Aspartokinase-beta subunit; aspartate beta semialdehyde dehydrogenase	Kalinowski, J. et al. "Genetic and biochemical analysis of the Aspartokinase from <i>Corynebacterium glutamicum</i> ," <i>Mol. Microbiol.</i> , 5(5):1197-1204 (1991); Kalinowski, J. et al. "Aspartokinase genes lysC alpha and lysC beta overlap and are adjacent to the aspartate beta-semialdehyde dehydrogenase gene asd in <i>Corynebacterium glutamicum</i> ," <i>Mol. Gen. Genet.</i> , 224(3):317-324 (1990)
X59403	gap;pgk; tpi	Glyceraldehyde-3-phosphate; phosphoglycerate kinase; triosephosphate isomerase	Eikmanns, B.J. "Identification, sequence analysis, and expression of a <i>Corynebacterium glutamicum</i> gene cluster encoding the three glycolytic enzymes glyceraldehyde-3-phosphate dehydrogenase, 3-phosphoglycerate kinase, and triosephosphate isomerase," <i>J. Bacteriol.</i> , 174(19):6076-6086 (1992)
X59404	gdh	Glutamate dehydrogenase	Bormann, E.R. et al. "Molecular analysis of the <i>Corynebacterium glutamicum</i> gdh gene encoding glutamate dehydrogenase," <i>Mol. Microbiol.</i> , 6(3):317-326 (1992)
X60312	lysI	L-lysine permease	Seep-Feldhaus, A.H. et al. "Molecular analysis of the <i>Corynebacterium glutamicum</i> lysI gene involved in lysine uptake," <i>Mol. Microbiol.</i> , 5(12):2995-3005 (1991)
X66078	copI	Psl protein	Joliff, G. et al. "Cloning and nucleotide sequence of the <i>espI</i> gene encoding Psl, one of the two major secreted proteins of <i>Corynebacterium glutamicum</i> : The deduced N-terminal region of Psl is similar to the <i>Mycobacterium antigen 85</i> complex," <i>Mol. Microbiol.</i> , 6(16):2349-2362 (1992)
X66112	glt	Citrate synthase	Eikmanns, B.J. et al. "Cloning sequence, expression and transcriptional analysis of the <i>Corynebacterium glutamicum</i> gltA gene encoding citrate synthase," <i>Microbiol.</i> , 140:1817-1828 (1994)
X67737	dapB	Dihydrodipicolinate reductase	
X69103	csp2	Surface layer protein PS2	Peyret, J.L. et al. "Characterization of the <i>cspB</i> gene encoding PS2, an ordered surface-layer protein in <i>Corynebacterium glutamicum</i> ," <i>Mol. Microbiol.</i> , 9(1):97-109 (1993)
X69104		IS3 related insertion element	Bonamy, C. et al. "Identification of IS1206, a <i>Corynebacterium glutamicum</i> IS3-related insertion sequence and phylogenetic analysis," <i>Mol. Microbiol.</i> , 14(3):571-581 (1994)

Table 2 (continued)

	leuA	Isopropylmalate synthase	
X70959			Patek, M. et al. "Leucine synthesis in <i>Corynebacterium glutamicum</i> : enzyme activities, structure of leuA, and effect of leuA inactivation on lysine synthesis," <i>Appl. Environ. Microbiol.</i> , 60(1):133-140 (1994)
X71489	icd	Isocitrate dehydrogenase (NADP+)	Eikmanns, B.J. et al. "Cloning sequence analysis, expression, and inactivation of the <i>Corynebacterium glutamicum</i> icd gene encoding isocitrate dehydrogenase and biochemical characterization of the enzyme," <i>J. Bacteriol.</i> , 177(3):774-782 (1995)
X72855	GDHA	Glutamate dehydrogenase (NADP+)	
X75083, X70584	mttA	5-methyltryptophan resistance	Heery, D.M. et al. "A sequence from a tryptophan-hyperproducing strain of <i>Corynebacterium glutamicum</i> encoding resistance to 5-methyltryptophan," <i>Biochem. Biophys. Res. Commun.</i> , 201(3):1255-1262 (1994)
X75085	recA		Fitzpatrick, R. et al. "Construction and characterization of recA mutant strains of <i>Corynebacterium glutamicum</i> and <i>Brevibacterium lactofermentum</i> ," <i>Appl. Microbiol. Biotechnol.</i> , 42(4):575-580 (1994)
X75504	aceA; thiX	Partial Isocitrate lyase; ?	Reinscheid, D.J. et al. "Characterization of the isocitrate lyase gene from <i>Corynebacterium glutamicum</i> and biochemical analysis of the enzyme," <i>J. Bacteriol.</i> , 176(12):3474-3483 (1994)
X76875		ATPase beta-subunit	Ludwig, W. et al. "Phylogenetic relationships of bacteria based on comparative sequence analysis of elongation factor Tu and ATP-synthase beta-subunit genes," <i>Antonie Van Leeuwenhoek</i> , 64:285-305 (1993)
X77034	tuf	Elongation factor Tu	Ludwig, W. et al. "Phylogenetic relationships of bacteria based on comparative sequence analysis of elongation factor Tu and ATP-synthase beta-subunit genes," <i>Antonie Van Leeuwenhoek</i> , 64:285-305 (1993)
X77384	recA		Billman-Jacobe, H. "Nucleotide sequence of a recA gene from <i>Corynebacterium glutamicum</i> ," <i>DNA Seq.</i> , 4(6):403-404 (1994)
X78491	aceB	Malate synthase	Reinscheid, D.J. et al. "Malate synthase from <i>Corynebacterium glutamicum</i> pta-ack operon encoding phosphotransacetylase: sequence analysis," <i>Microbiology</i> , 140:3099-3108 (1994)
X80629	16S rDNA	16S ribosomal RNA	Rainey, F.A. et al. "Phylogenetic analysis of the genera <i>Rhodococcus</i> and <i>Norcardia</i> and evidence for the evolutionary origin of the genus <i>Norcardia</i> from within the radiation of <i>Rhodococcus</i> species," <i>Microbiol.</i> , 141:523-528 (1995)
X81191	gluA; gluB; gluC; gluD	Glutamate uptake system	Kronmeyer, W. et al. "Structure of the gluABCD cluster encoding the glutamate uptake system of <i>Corynebacterium glutamicum</i> ," <i>J. Bacteriol.</i> , 177(5):1152-1158 (1995)
X81379	dapE	Succinyl-diaminopimelate desuccinylase	Wehrmann, A. et al. "Analysis of different DNA fragments of <i>Corynebacterium glutamicum</i> complementing dapE of <i>Escherichia coli</i> ," <i>Microbiology</i> , 40:3349-56 (1994)

Table 2 (continued)

X82061	16S rDNA	16S ribosomal RNA	Ruimy, R. et al. "Phylogeny of the genus <i>Corynebacterium</i> deduced from analyses of small-subunit ribosomal DNA sequences," <i>Int. J. Syst. Bacteriol.</i> , 45(4):740-746 (1995)
X82928	asd, ysc	Aspartate-semialdehyde dehydrogenase; ?	Serebrijski, I. et al. "Multicopy suppression by <i>asd</i> gene and osmotic stress-dependent complementation by heterologous <i>proA</i> in <i>proA</i> mutants," <i>J. Bacteriol.</i> , 177(24):7255-7260 (1995)
X82929	proA	Gamma-glutamyl-phosphate reductase	Serebrijski, I. et al. "Multicopy suppression by <i>asd</i> gene and osmotic stress-dependent complementation by heterologous <i>proA</i> in <i>proA</i> mutants," <i>J. Bacteriol.</i> , 177(24):7255-7260 (1995)
X84257	16S rDNA	16S ribosomal RNA	Pascual, C. et al. "Phylogenetic analysis of the genus <i>Corynebacterium</i> based on 16S rRNA gene sequences," <i>Int. J. Syst. Bacteriol.</i> , 45(4):724-728 (1995)
X85965	aroP, dapE	Aromatic amino acid permease; ?	Wehrmann et al. "Functional analysis of sequences adjacent to <i>dapE</i> of <i>C. glutamicum</i> proline reveals the presence of <i>aroP</i> , which encodes the aromatic amino acid transporter," <i>J. Bacteriol.</i> , 177(20):5991-5993 (1995)
X86157	argB, argC, argD, argF, argJ	Acetylglutamate kinase; N-acetyl-gamma-glutamyl-phosphate reductase; acetylornithine aminotransferase; ornithine carbamoyltransferase; glutamate N-acetyltransferase	Sakanyan, V. et al. "Genes and enzymes of the acetyl cycle of arginine biosynthesis in <i>Corynebacterium glutamicum</i> : enzyme evolution in the early steps of the arginine pathway," <i>Microbiology</i> , 142:99-108 (1996)
X89084	pta, ackA	Phosphate acetyltransferase; acetate kinase	Reinscheid, D.J. et al. "Cloning, sequence analysis, expression and inactivation of the <i>Corynebacterium glutamicum</i> <i>pta-ack</i> operon encoding phosphotransacetylase and acetate kinase," <i>Microbiology</i> , 145:503-513 (1999)
X89830	attB	Attachment site	Le Marrec, C. et al. "Genetic characterization of site specific integration functions of phi AAU2 infecting 'Arthrobacter aureus C70,'" <i>J. Bacteriol.</i> , 178(7):1996-2004 (1996)
X90356		Promoter fragment F1	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90357		Promoter fragment F2	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90358		Promoter fragment F10	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90359		Promoter fragment F13	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)

Table 2 (continued)

X90360	Promoter fragment F22	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90361	Promoter fragment F34	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90362	Promoter fragment F37	Patek, M. et al. "Promoters from <i>C. glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90363	Promoter fragment F45	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90364	Promoter fragment F64	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90365	Promoter fragment F75	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90366	Promoter fragment PF101	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90367	Promoter fragment PF104	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90368	Promoter fragment PF109	Patek, M. et al. "Promoters from <i>Corynebacterium glutamicum</i> : cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X93513	Ammonium transport system	Siewe, R.M. et al. "Functional and genetic characterization of the (methyl) ammonium uptake carrier of <i>Corynebacterium glutamicum</i> ," <i>J. Biol. Chem.</i> , 271(10):5398-5403 (1996)
X93514	Glycine betaine transport system	Peter, H. et al. "Isolation, characterization, and expression of the <i>Corynebacterium glutamicum</i> betP gene, encoding the transport system for the compatible solute glycine betaine," <i>J. Bacteriol.</i> , 178(17):5229-5234 (1996)
X95649		Patek, M. et al. "Identification and transcriptional analysis of the dapB-ORF2-dapA-ORF4 operon of <i>Corynebacterium glutamicum</i> , encoding two enzymes involved in L-lysine synthesis," <i>Biotechnol. Lett.</i> , 19:1113-1117 (1997)
X96471	Lysine exporter protein; Lysine export regulator protein	Vrijic, M. et al. "A new type of transporter with a new type of cellular function: L-lysine export from <i>Corynebacterium glutamicum</i> ," <i>Mol. Microbiol.</i> , 22(5):815-826 (1996)

Table 2 (continued)

X96580	panB, panC, xylB	3-methyl-2-oxobutanoate hydroxymethyltransferase; pantoate-beta-alanine ligase; xylulokinase	Sahm, H. et al. "D-pantothenate synthesis in Corynebacterium glutamicum and use of panBC and genes encoding L-valine synthesis for D-pantothenate overproduction," <i>Appl. Environ. Microbiol.</i> , 65(5):1973-1979 (1999)
X96962		Insertion sequence IS1207 and transposase	
X99289		Elongation factor P	Ramos, A. et al. "Cloning, sequencing and expression of the gene encoding elongation factor P in the amino-acid producer Brevibacterium lactofermentum (Corynebacterium glutamicum ATCC 13869)," <i>Gene</i> , 198:217-222 (1997)
Y00140	thrB	Homoserine kinase	Mateos, L.M. et al. "Nucleotide sequence of the homoserine kinase (thrB) gene of the Brevibacterium lactofermentum," <i>Nucleic Acids Res.</i> , 15(9):3922 (1987)
Y00151	ddh	Meso-diaminopimelate D-dehydrogenase (EC 1.4.1.16)	Ishino, S. et al. "Nucleotide sequence of the meso-diaminopimelate D-dehydrogenase gene from Corynebacterium glutamicum," <i>Nucleic Acids Res.</i> , 15(9):3917 (1987)
Y00476	thrA	Homoserine dehydrogenase	Mateos, L.M. et al. "Nucleotide sequence of the homoserine dehydrogenase (thrA) gene of the Brevibacterium lactofermentum," <i>Nucleic Acids Res.</i> , 15(24):10598 (1987)
Y00546	hom; thrB	Homoserine dehydrogenase; homoserine kinase	Peoples, O.P. et al. "Nucleotide sequence and fine structural analysis of the Corynebacterium glutamicum hom-thrB operon," <i>Mol. Microbiol.</i> , 2(1):63-72 (1988)
Y08964	murC; ftsQ/divD; ftsZ	UPD-N-acetylmuramate-alanine ligase; division initiation protein or cell division protein; cell division protein	Honrubia, M.P. et al. "Identification, characterization, and chromosomal organization of the ftsZ gene from Brevibacterium lactofermentum," <i>Mol. Gen. Genet.</i> , 259(1):97-104 (1998)
Y09163	putP	High affinity proline transport system	Peter, H. et al. "Isolation of the putP gene of Corynebacterium glutamicum proline and characterization of a low-affinity uptake system for compatible solutes," <i>Arch. Microbiol.</i> , 168(2):143-151 (1997)
Y09548	pyc	Pyruvate carboxylase	Peters-Wendisch, P.G. et al. "Pyruvate carboxylase from Corynebacterium glutamicum: characterization, expression and inactivation of the pyc gene," <i>Microbiology</i> , 144:915-927 (1998)
Y09578	leuB	3-isopropylmalate dehydrogenase	Patek, M. et al. "Analysis of the leuB gene from Corynebacterium glutamicum," <i>Appl. Microbiol. Biotechnol.</i> , 50(1):42-47 (1998)
Y12472		Attachment site bacteriophage Phi-16	Moreau, S. et al. "Site-specific integration of coryneophage Phi-16: The construction of an integration vector," <i>Microbiol.</i> , 145:539-548 (1999)
Y12537	proP	Proline/ectoine uptake system protein	Peter, H. et al. "Corynebacterium glutamicum is equipped with four secondary carriers for compatible solutes: Identification, sequencing, and characterization of the proline/ectoine uptake system, ProP, and the ectoine/proline/glycine betaine carrier, EctP," <i>J. Bacteriol.</i> , 180(22):6005-6012 (1998)

Table 2 (continued)

Y13221	glnA	Glutamine synthetase I	Jakoby, M. et al. "Isolation of Corynebacterium glutamicum glnA gene encoding glutamine synthetase I," <i>FEMS Microbiol. Lett.</i> , 154(1):81-88 (1997)
Y16642	lpd	Dihydrolipoamide dehydrogenase	
Y18059		Attachment site Corynebacterium 304L	
Z21501	argS; lysA	Arginyl-tRNA synthetase; diaminopimelate decarboxylase (partial)	Moreau, S. et al. "Analysis of the integration functions of φ304L: An integrase module among corynebacteriophages," <i>Virology</i> , 255(1):150-159 (1999)
Z21502	dapA; dapB	Dihydrodipicolinate synthase; dihydrodipicolinate reductase	Oguiza, J.A. et al. "A gene encoding arginyl-tRNA synthetase is located in the upstream region of the lysA gene in Brevibacterium lactofermentum: Regulation of argS-lysA cluster expression by arginine," <i>J. Bacteriol.</i> , 175(22):7356-7362 (1993)
Z29563	thrC	Threonine synthase	Pisabarro, A. et al. "A cluster of three genes (dapA, orf2, and dapB) of Brevibacterium lactofermentum encodes dihydrodipicolinate reductase, and a third polypeptide of unknown function," <i>J. Bacteriol.</i> , 175(9):2743-2749 (1993)
Z46753	16S rDNA	Gene for 16S ribosomal RNA	Malumbres, M. et al. "Analysis and expression of the thrC gene of the encoded threonine synthase," <i>Appl. Environ. Microbiol.</i> , 60(7):2209-2219 (1994)
Z49822	sigA	SigA sigma factor	Oguiza, J.A. et al. "Multiple sigma factor genes in Brevibacterium lactofermentum: Characterization of sigA and sigB," <i>J. Bacteriol.</i> , 178(2):550-553 (1996)
Z49823	galE; dixR	Catalytic activity UDP-galactose 4-epimerase; diphtheria toxin regulatory protein	Oguiza, J.A. et al. "The galE gene encoding the UDP-galactose 4-epimerase of Brevibacterium lactofermentum is coupled transcriptionally to the dmdR gene," <i>Gene</i> , 177:103-107 (1996)
Z49824	orf1; sigB	?; SigB sigma factor	Oguiza, J.A. et al. "Multiple sigma factor genes in Brevibacterium lactofermentum: Characterization of sigA and sigB," <i>J. Bacteriol.</i> , 178(2):550-553 (1996)
Z66534		Transposase	Correia, A. et al. "Cloning and characterization of an IS-like element present in the genome of Brevibacterium lactofermentum ATCC 13869," <i>Gene</i> , 170(1):91-94 (1996)
A sequence for this gene was published in the indicated reference. However, the sequence obtained by the inventors of the present application is significantly longer than the published version. It is believed that the published version relied on an incorrect start codon, and thus represents only a fragment of the actual coding region.			

TABLE 3: Corynebacterium and Brevibacterium Strains Which May be Used in the Practice of the Invention

Genus	Species	ATCC	FERM	NRRL	CECT	NCIMB	CBS	NCTC	DSMZ
Brevibacterium	ammoniagenes	21054							
Brevibacterium	ammoniagenes	19350							
Brevibacterium	ammoniagenes	19351							
Brevibacterium	ammoniagenes	19352							
Brevibacterium	ammoniagenes	19353							
Brevibacterium	ammoniagenes	19354							
Brevibacterium	ammoniagenes	19355							
Brevibacterium	ammoniagenes	19356							
Brevibacterium	ammoniagenes	21055							
Brevibacterium	ammoniagenes	21077							
Brevibacterium	ammoniagenes	21553							
Brevibacterium	ammoniagenes	21580							
Brevibacterium	ammoniagenes	39101							
Brevibacterium	butanicum	21196							
Brevibacterium	divaricatum	21792	P928						
Brevibacterium	flavum	21474							
Brevibacterium	flavum	21129							
Brevibacterium	flavum	21518							
Brevibacterium	flavum			B11474					
Brevibacterium	flavum			B11472					
Brevibacterium	flavum	21127							
Brevibacterium	flavum	21128							
Brevibacterium	flavum	21427							
Brevibacterium	flavum	21475							
Brevibacterium	flavum	21517							
Brevibacterium	flavum	21528							
Brevibacterium	flavum	21529							
Brevibacterium	flavum			B11477					
Brevibacterium	flavum			B11478					
Brevibacterium	flavum	21127							
Brevibacterium	flavum			B11474					
Brevibacterium	healii	15527							
Brevibacterium	ketoglutamicum	21004							
Brevibacterium	ketoglutamicum	21089							
Brevibacterium	ketosoreductum	21914							
Brevibacterium	lactofermentum				70				
Brevibacterium	lactofermentum				74				
Brevibacterium	lactofermentum				77				
Brevibacterium	lactofermentum	21798							
Brevibacterium	lactofermentum	21799							
Brevibacterium	lactofermentum	21800							
Brevibacterium	lactofermentum	21801							
Brevibacterium	lactofermentum			B11470					
Brevibacterium	lactofermentum			B11471					

Genus	species	ATCC	FERM	NRRL	CECT	NCIMB	CBS	NCTC	DSMZ
Brevibacterium	lactofermentum	21086							
Brevibacterium	lactofermentum	21420							
Brevibacterium	lactofermentum	21086							
Brevibacterium	lactofermentum	31269							
Brevibacterium	linens	9174							
Brevibacterium	linens	19391							
Brevibacterium	linens	8377							
Brevibacterium	paraffinolyticum					11160			
Brevibacterium	spec.						717.73		
Brevibacterium	spec.						717.73		
Brevibacterium	spec.	14604							
Brevibacterium	spec.	21860							
Brevibacterium	spec.	21864							
Brevibacterium	spec.	21865							
Brevibacterium	spec.	21866							
Brevibacterium	spec.	19240							
Corynebacterium	acetoacidophilum	21476							
Corynebacterium	acetoacidophilum	13870							
Corynebacterium	acetoglutamicum			B11473					
Corynebacterium	acetoglutamicum			B11475					
Corynebacterium	acetoglutamicum	15806							
Corynebacterium	acetoglutamicum	21491							
Corynebacterium	acetoglutamicum	31270							
Corynebacterium	acetophilum			B3671					
Corynebacterium	ammoniagenes	6872						2399	
Corynebacterium	ammoniagenes	15511							
Corynebacterium	fujikense	21496							
Corynebacterium	glutamicum	14067							
Corynebacterium	glutamicum	39137							
Corynebacterium	glutamicum	21254							
Corynebacterium	glutamicum	21255							
Corynebacterium	glutamicum	31830							
Corynebacterium	glutamicum	13032							
Corynebacterium	glutamicum	14305							
Corynebacterium	glutamicum	15455							
Corynebacterium	glutamicum	13058							
Corynebacterium	glutamicum	13059							
Corynebacterium	glutamicum	13060							
Corynebacterium	glutamicum	21492							
Corynebacterium	glutamicum	21513							
Corynebacterium	glutamicum	21526							
Corynebacterium	glutamicum	21543							
Corynebacterium	glutamicum	13287							
Corynebacterium	glutamicum	21851							
Corynebacterium	glutamicum	21253							
Corynebacterium	glutamicum	21514							
Corynebacterium	glutamicum	21516							
Corynebacterium	glutamicum	21299							

Genus	species	ATCC	FERM	NRRL	CECT	NCIMB	CBS	NCIC	DSMZ
Corynebacterium	glutamicum	21300							
Corynebacterium	glutamicum	39684							
Corynebacterium	glutamicum	21488							
Corynebacterium	glutamicum	21649							
Corynebacterium	glutamicum	21650							
Corynebacterium	glutamicum	19223							
Corynebacterium	glutamicum	13869							
Corynebacterium	glutamicum	21157							
Corynebacterium	glutamicum	21158							
Corynebacterium	glutamicum	21159							
Corynebacterium	glutamicum	21355							
Corynebacterium	glutamicum	31808							
Corynebacterium	glutamicum	21674							
Corynebacterium	glutamicum	21562							
Corynebacterium	glutamicum	21563							
Corynebacterium	glutamicum	21564							
Corynebacterium	glutamicum	21565							
Corynebacterium	glutamicum	21566							
Corynebacterium	glutamicum	21567							
Corynebacterium	glutamicum	21568							
Corynebacterium	glutamicum	21569							
Corynebacterium	glutamicum	21570							
Corynebacterium	glutamicum	21571							
Corynebacterium	glutamicum	21572							
Corynebacterium	glutamicum	21573							
Corynebacterium	glutamicum	21579							
Corynebacterium	glutamicum	19049							
Corynebacterium	glutamicum	19050							
Corynebacterium	glutamicum	19051							
Corynebacterium	glutamicum	19052							
Corynebacterium	glutamicum	19053							
Corynebacterium	glutamicum	19054							
Corynebacterium	glutamicum	19055							
Corynebacterium	glutamicum	19056							
Corynebacterium	glutamicum	19057							
Corynebacterium	glutamicum	19058							
Corynebacterium	glutamicum	19059							
Corynebacterium	glutamicum	19060							
Corynebacterium	glutamicum	19185							
Corynebacterium	glutamicum	13286							
Corynebacterium	glutamicum	21515							
Corynebacterium	glutamicum	21527							
Corynebacterium	glutamicum	21544							
Corynebacterium	glutamicum	21492							
Corynebacterium	glutamicum			B8183					
Corynebacterium	glutamicum			B8182					
Corynebacterium	glutamicum			B12416					
Corynebacterium	glutamicum			B12417					

Genus	species	ATCC	FERM	NRRL	CECT	NCIMB	CBS	NCTC	DSMZ
Corynebacterium	glutamicum			B12418					
Corynebacterium	glutamicum			B11476					
Corynebacterium	glutamicum	21608							
Corynebacterium	lilium		P973						
Corynebacterium	nitrilophilus	21419				11594			
Corynebacterium	spec.		P4445						
Corynebacterium	spec.		P4446						
Corynebacterium	spec.	31088							
Corynebacterium	spec.	31089							
Corynebacterium	spec.	31090							
Corynebacterium	spec.	31090							
Corynebacterium	spec.	31090							
Corynebacterium	spec.	15954							20145
Corynebacterium	spec.	21857							
Corynebacterium	spec.	21862							
Corynebacterium	spec.	21863							

ATCC: American Type Culture Collection, Rockville, MD, USA

FERM: Fermentation Research Institute, Chiba, Japan

NRRL: ARS Culture Collection, Northern Regional Research Laboratory, Peoria, IL, USA

CECT: Coleccion Espanola de Cultivos Tipo, Valencia, Spain

NCIMB: National Collection of Industrial and Marine Bacteria Ltd., Aberdeen, UK

CBS: Centraalbureau voor Schimmelcultures, Baarn, NL

NCTC: National Collection of Type Cultures, London, UK

DSMZ: Deutsche Sammlung von Mikroorganismen und Zellkulturen, Braunschweig, Germany

For reference see Sugawara, H. et al. (1993) World directory of collections of cultures of microorganisms: Bacteria, fungi and yeasts (4th edn), World federation for culture collections world data center on microorganisms, Saimata, Japan.

Table 4: Alignment Results

ID #	length (NT)	Genbank Hit	Length	Accession	Name of Genbank Hit	Source of Genbank Hit	% homology (GAP)	Date of Deposit
αa00023	3579	GB_EST33:AI776129	483	AI776129	EST257217 tomato resistant, Cornell Lycopersicon esculentum cDNA clone cLER17D3, mRNA sequence.	Lycopersicon esculentum	40,956	29-Jun-99
		GB_EST33:AI776129	483	AI776129	EST257217 tomato resistant, Cornell Lycopersicon esculentum cDNA clone cLER17D3, mRNA sequence.	Lycopersicon esculentum	40,956	29-Jun-99
αa00044	1059	EM_PAT:E11760	6911	E11760	Base sequence of sucrase gene.	Corynebacterium glutamicum	42,979	08-OCT- 1997 (Rel. 52, Created) 07-OCT- 1996
		GB_PAT:26124	6911	I26124	Sequence 4 from patent US 5556776.	Unknown.	42,979	17-DEC- 1993
αa00064	1401	GB_BA2:ECOUW89	176195	U00006	E. coli chromosomal region from 89.2 to 92.8 minutes.	Escherichia coli	39,097	28-Jul-99
		GB_PAT:E16763	2517	E16763	gDNA encoding aspartate transferase (AAT).	Corynebacterium glutamicum	95,429	2-Aug-99
αa00072		GB_HTG2:AC007892	134257	AC007892	Drosophila melanogaster chromosome 3 clone BACR02003 (D797) RPCI-98 02.O.3 map 99B-99B strain y; cn bw sp. *** SEQUENCING IN PROGRESS ***, 113 unordered pieces.	Drosophila melanogaster	31,111	2-Aug-99
		GB_HTG2:AC007892	134257	AC007892	Drosophila melanogaster chromosome 3 clone BACR02003 (D797) RPCI-98 02.O.3 map 99B-99B strain y; cn bw sp. *** SEQUENCING IN PROGRESS***, 113 unordered pieces.	Drosophila melanogaster	31,111	2-Aug-99
αa00105	798	GB_BA1:MTV002	56414	AL008967	Mycobacterium tuberculosis H37Rv complete genome, segment 122/162.	Mycobacterium tuberculosis	37,753	17-Jun-98
		GB_BA1:ECU29581	71128	U29581	Escherichia coli K-12 genome; approximately 63 to 64 minutes.	Escherichia coli	35,669	14-Jan-97
αa00106	579	GB_BA2:AE000366	10405	AE000366	Escherichia coli K-12 MG1655 section 256 of 400 of the complete genome.	Escherichia coli	35,669	12-Nov-98
		GB_EST15:AA494237	367	AA494237	ng83D04.s1 NCI_CGAP_P16 Homo sapiens cDNA clone IMAGE:941407 similar to SW:DIYR_LACCA P00381 DIHYDROFOLATE REDUCTASE ;, mRNA sequence.	Homo sapiens	42,896	20-Aug-97
αa00115	1170	GB_BA2:AF161327	2021	AF161327	Corynebacterium diphtheriae histidine kinase ChrS (chrS) and response regulator ChrA (chrA) genes, complete cds.	Corynebacterium diphtheriae	40,210	9-Sep-99
		GB_PAT:AR041189	654	AR041189	Sequence 4 from patent US 5811286.	Unknown.	41,176	29-Sep-99
		GB_PR4:AC007110	148336	AC007110	Homo sapiens chromosome 17, clone hRPK 472_J_18, complete sequence.	Homo sapiens	36,783	30-MAR- 1999
		GB_HTG3:AC008537	170030	AC008537	Homo sapiens chromosome 19 clone CIT-HSPC_490E21, *** SEQUENCING IN PROGRESS ***; 93 unordered pieces.	Homo sapiens	40,296	2-Sep-99
		GB_HTG3:AC008537	170030	AC008537	Homo sapiens chromosome 19 clone CIT-HSPC_490E21, *** SEQUENCING IN PROGRESS ***; 93 unordered pieces.	Homo sapiens	40,296	2-Sep-99

Table 4 (continued)

Accession	GB	Accession	Accession	Accession	Description	Accession	Date
αa00116	1284	GB_BA2.AF062345	16458	AF062345	Caulobacter crescentus SstI (sst1), S-layer protein subunit (rsaA), ABC transporter (rsaD), membrane forming unit (rsaE), putative GDP-mannose-4,6-dehydratase (psaA), putative acetyltransferase (psb), putative perosamine synthetase (psC), putative mannitoltransferase (psD), putative mannitoltransferase (psE), outer membrane protein (rsaF), and putative perosamine transferase (psE) genes, complete cds. Sequence 6 from patent US 5500353.	Caulobacter crescentus	19-OCT-1999
		GB_PAT.118647	3300	118647		Unknown.	07-OCT-1996
αa00131	732	GB_GSS13.AQ44619	751	AQ44619	nbxb0062D16r CUGI Rice BAC Library Oryza sativa genomic clone nbxb0062D16r, genomic survey sequence.	Oryza sativa	8-Apr-99
		GB_BA1.MTY20811	36330	Z95121	Mycobacterium tuberculosis H37Rv complete genome; segment 139/162.	Mycobacterium tuberculosis	17-Jun-98
		GB_BA1.SAR7932	15176	AJ007932	Streptomyces argillaceus mithramycin biosynthetic genes.	Streptomyces argillaceus	15-Jun-99
		GB_BA1.MTY20811	36330	Z95121	Mycobacterium tuberculosis H37Rv complete genome; segment 139/162.	Mycobacterium tuberculosis	17-Jun-98
αa00132	1557	GB_BA1.MTY20811	36330	Z95121	Mycobacterium tuberculosis H37Rv complete genome; segment 139/162.	Mycobacterium tuberculosis	17-Jun-98
		GB_IN2.TVU40872	1882	U40872	Trichomonas vaginalis S-adenosyl-L-homocysteine hydrolase gene, complete cds.	Trichomonas vaginalis	31-OCT-1996
		GB_HTG6.AC010706	169265	AC010706	Drosophila melanogaster chromosome X clone BACR36D15 (D887) RPCI-98 36 D.15 map 13C-13E strain y; cn bw sp. *** SEQUENCING IN PROGRESS ***; 74 unordered pieces.	Drosophila melanogaster	22-Nov-99
αa00145	1059	GB_BA1.MTCY2B12	20431	Z81011	Mycobacterium tuberculosis H37Rv complete genome; segment 61/162.	Mycobacterium tuberculosis	18-Jun-98
		GB_BA1.PSEPYRBX	2273	L19649	Pseudomonas aeruginosa aspartate transcarbamoylase (pyrB) and dihydroorotase-like (pyrX) genes, complete cds's.	Pseudomonas aeruginosa	26-Jul-93
		GB_BA1.LLPYRBDNA	1468	X84262	L. leichmannii pyrB gene.	Lactobacillus leichmannii	29-Apr-97
αa00146	1464	GB_BA1.MTCY2B12	20431	Z81011	Mycobacterium tuberculosis H37Rv complete genome; segment 61/162.	Mycobacterium tuberculosis	18-Jun-98
		GB_BA1.MTCY154	13935	Z98209	Mycobacterium tuberculosis H37Rv complete genome; segment 121/162.	Mycobacterium tuberculosis	17-Jun-98
		GB_BA1.MSGY154	40221	AD000002	Mycobacterium tuberculosis sequence from clone y154.	Mycobacterium tuberculosis	03-DEC-1996
αa00147	1302	GB_BA1.MTCY2B12	20431	Z81011	Mycobacterium tuberculosis H37Rv complete genome; segment 61/162.	Mycobacterium tuberculosis	18-Jun-98
		GB_BA1.MSG8937C	38914	L78820	Mycobacterium leprae cosmid B937 DNA sequence.	Mycobacterium leprae	15-Jun-96
		GB_BA1.PAU81259	7285	U81259	Pseudomonas aeruginosa dihydrodipicolinate reductase (dapB) gene, partial cds, carbamoylphosphate synthetase small subunit (carA) and carbamoylphosphate synthetase large subunit (carB) genes, complete cds, and FtsJ homolog (ftsJ) gene, partial cds.	Pseudomonas aeruginosa	23-DEC-1996
αa00156	1233	GB_BA1.SC9810	33320	AL009204	Streptomyces coelicolor cosmid 9B10.	Streptomyces coelicolor	10-Feb-99

Table 4 (continued)

GB_BA2.AF002133	15437	AF002133	Mycobacterium avium strain GIR10 transcriptional regulator (mav81) gene, partial cds, aconitase (acn), invasin 1 (inv1), invasin 2 (inv2), transcriptional regulator (moxR), ketoacyl-reductase (fabG), enoyl-reductase (inhA) and ferrochelatase (mav272) genes, complete cds.	Mycobacterium avium	54,191	26-MAR-1998
GB_BA1.D85417	7984	D85417	Propionibacterium freudenreichii hemY, hemH, hemB, hemX, hemR and hemL genes, complete cds.	Propionibacterium freudenreichii	46,667	6-Feb-99
GB_HTG3.AC008167	174223	AC008167	Homo sapiens clone NH0172013, *** SEQUENCING IN PROGRESS ***; 7 unordered pieces.	Homo sapiens	37,451	21-Aug-99
GB_HTG3.AC008167	174223	AC008167	Homo sapiens clone NH0172013, *** SEQUENCING IN PROGRESS ***; 7 unordered pieces.	Homo sapiens	37,451	21-Aug-99
GB_HTG4.AC010118	80605	AC010118	Drosophila melanogaster chromosome 3L/62B1 clone RPC198-10D15, *** SEQUENCING IN PROGRESS ***; 51 unordered pieces.	Drosophila melanogaster	38,627	16-OCT-1999
GB_BA1.AB024708	8734	AB024708	Corynebacterium glutamicum gltB and gltD genes for glutamine 2-oxoglutarate aminotransferase large and small subunits, complete cds.	Corynebacterium glutamicum	92,113	13-MAR-1999
GB_BA1.AB024708	8734	AB024708	Corynebacterium glutamicum gltB and gltD genes for glutamine 2-oxoglutarate aminotransferase large and small subunits, complete cds.	Corynebacterium glutamicum	93,702	13-MAR-1999
GB_EST24.A1232702	528	A1232702	EST229390 Normalized rat kidney, Bento Soares Rattus sp. cDNA clone RKICF35 3' end, mRNA sequence.	Rattus sp.	34,221	31-Jan-99
GB_HTG2.HSDJ850E	117353	AL121758	Homo sapiens chromosome 20 clone RP5-850E9, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	37,965	03-DEC-1999
GB_HTG2.HSDJ850E	117353	AL121758	Homo sapiens chromosome 20 clone RP5-850E9, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	37,965	03-DEC-1999
GB_PR2.CNS01DSA	159400	AL121766	Human chromosome 14 DNA sequence *** IN PROGRESS *** BAC R-412H8 of RPC1-11 library from chromosome 14 of Homo sapiens (Human), complete sequence.	Homo sapiens	38,796	11-Nov-99
GB_HTG2.AC005079	110000	AC005079	Homo sapiens clone RG252P22, *** SEQUENCING IN PROGRESS ***; 3 unordered pieces.	Homo sapiens	38,227	22-Nov-98
GB_HTG2.AC005079	110000	AC005079	Homo sapiens clone RG252P22, *** SEQUENCING IN PROGRESS ***; 3 unordered pieces.	Homo sapiens	38,227	22-Nov-98
GB_HTG2.AC005079	110000	AC005079	Homo sapiens clone RG252P22, *** SEQUENCING IN PROGRESS ***; 3 unordered pieces.	Homo sapiens	38,227	22-Nov-98
GB_BA1.PPEA3NIF	19771	X99694	Plasmid pEA3 nitrogen fixation genes.	Enterobacter agglomerans	48,826	2-Aug-96
GB_BA2.AF128444	2477	AF128444	Rhodobacter capsulatus molybdenum cofactor biosynthetic gene cluster, partial sequence.	Rhodobacter capsulatus	40,135	22-MAR-1999
GB_HTG4.AC010111	138938	AC010111	Drosophila melanogaster chromosome 3L/70C1 clone RPC198-9B18, *** SEQUENCING IN PROGRESS ***; 64 unordered pieces.	Drosophila melanogaster	39,527	16-OCT-1999
GB_BA2.AF124518	1758	AF124518	Corynebacterium glutamicum 3-dehydroquinase (aroD) and shikimate dehydrogenase (aroE) genes, complete cds.	Corynebacterium glutamicum	98,237	18-MAY-1999
GB_PR3.AC004593	150221	AC004593	Homo sapiens PAC clone DJ0964C11 from 7p14-p15, complete sequence.	Homo sapiens	36,616	18-Apr-98
GB_HTG2.AC006907	188972	AC006907	Caenorhabditis elegans clone Y76B12, *** SEQUENCING IN PROGRESS ***; 25 unordered pieces.	Caenorhabditis elegans	37,095	26-Feb-99
GB_BA1.CGLYSI	4232	X60312	C. glutamicum lysI gene for L-lysine permease.	Corynebacterium glutamicum	100,000	30-Jan-92

Table 4 (continued)

	GB_HTG1:PFMAL13P 192581	AL049180	Plasmodium falciparum chromosome 13 strain 3D7, *** SEQUENCING IN PROGRESS *** in unordered pieces.	34,947	11-Aug-99
	GB_HTG1:PFMAL13P 192581	AL049180	Plasmodium falciparum chromosome 13 strain 3D7, *** SEQUENCING IN PROGRESS *** in unordered pieces.	34,947	11-Aug-99
rx00262	GB_IN2:EHU89655 3219	U89655	Entamoeba histolytica unconventional myosin IB mRNA, complete cds.	36,496	23-MAY-1997
	GB_IN2:EHU89655 3219	U89655	Entamoeba histolytica unconventional myosin IB mRNA, complete cds.	37,544	23-MAY-1997
rx00266	GB_RO:AF016190 2939	AF016190	Mus musculus connexin-36 (Cx36) gene, complete cds.	41,856	9-Feb-99
	EM_PAT:E09719 3505	E09719	DNA encoding precursor protein of alkaline cellulase.	34,741	08-OCT-1997 (Rel. 52, Created)
rx00278	GB_PAT:E02133 3494	E02133	gDNA encoding alkaline cellulase.	34,741	29-Sep-97
	GB_IN1:CELK05F6 36912	AF040653	Caenorhabditis elegans cosmid K05F6.	36,943	6-Jan-98
	GB_BA1:CGU43535 2531	U43535	Corynebacterium glutamicum multidrug resistance protein (cmr) gene, complete cds.	36,658	9-Apr-97
rx00295	GB_RO:RNU30789 3510	U30789	Rattus norvegicus clone N27 mRNA.	38,190	20-Aug-96
	GB_BA2:CGU31281 1614	U31281	Corynebacterium glutamicum biotin synthase (bioB) gene, complete cds.	99,111	21-Nov-96
	GB_BA1:BRLBIOBA 1647	D14084	Brevibacterium flavum gene for biotin synthetase, complete cds.	98,489	3-Feb-99
	GB_PAT:E03937 1005	E03937	DNA sequence encoding Brevibacterium flavum biotin-synthase.	98,207	29-Sep-97
rx00323	GB_BA1:MTCY427 38110	Z70692	Mycobacterium tuberculosis H37Rv complete genome, segment 99/162.	35,615	24-Jun-99
	GB_BA1:MSGB32CS 36404	L78818	Mycobacterium leprae cosmid B32 DNA sequence.	60,917	15-Jun-96
	GB_BA1:MTCY427 38110	Z70692	Mycobacterium tuberculosis H37Rv complete genome, segment 99/162.	44,606	24-Jun-99
rx00324	GB_BA1:MSGB32CS 36404	L78818	Mycobacterium leprae cosmid B32 DNA sequence.	52,516	15-Jun-96
	GB_BA1:MTCY427 38110	Z70692	Mycobacterium tuberculosis H37Rv complete genome, segment 99/162.	38,079	24-Jun-99
	GB_OM:BOVELA 3242	J02717	Bovine elastin a mRNA, complete cds.	39,351	27-Apr-93
rx00330	GB_BA1:CGTHRC 3120	X56037	Corynebacterium glutamicum thrC gene for threonine synthase (EC 4.2.99.2).	99,808	17-Jun-97
	GB_PAT:IO9078 3146	IO9078	Sequence 4 from Patent WO 8809819.	99,617	02-DEC-1994
	GB_BA1:BLTHRESY 1892	Z29563	Brevibacterium lactofermentum; ATCC 13869; DNA (genomic);.	99,170	20-Sep-95
rx00335	GB_BA1:CGGLNA 3686	Y13221	Corynebacterium glutamicum glnA gene.	100,000	28-Aug-97

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BNSDOCID: <WO__0100843A2 I >

Table 4 (continued)

rx00377	1245	GB_BA1.CCU13664	1678	U13664	Caulobacter crescentus uroporphyrinogen decarboxylase homolog (hemE) gene, partial cds.	Caulobacter crescentus	36,832	24-MAR-1995
		GB_PL1:ANSDGENE	1299	Y08866	A.nidulans sD gene.	Emericella nidulans	39,603	17-OCT-1996
rx00382	1425	GB_GSS4.AQ730303	483	AQ730303	HS_5505_B1_C04_T7A RPC1-11 Human Male BAC Library Homo sapiens genomic clone Plate=1081 Col=7 Row=F, genomic survey sequence.	Homo sapiens	36,728	15-JUN-99
		GB_BA1:PAHEML	4444	X82072	P.aeruginosa hemL gene.	Pseudomonas aeruginosa	54,175	18-DEC-1995
		GB_BA1.MTY25D10	40838	Z95558	Mycobacterium tuberculosis H37Rv complete genome, segment 28/162.	Mycobacterium tuberculosis	61,143	17-JUN-98
		GB_BA1.MSGY224	40051	AD000004	Mycobacterium tuberculosis sequence from clone y224.	Mycobacterium tuberculosis	61,143	03-DEC-1996
rx00383	1467	GB_BA1.MLCB1222	34714	AL049491	Mycobacterium leprae cosmid B1222.	Mycobacterium leprae	43,981	27-AUG-99
		GB_HTG2.AC006269	167171	AC006269	Homo sapiens chromosome 17 clone hRPK.515_E_23 map 17, *** SEQUENCING IN PROGRESS ***, 2 ordered pieces.	Homo sapiens	35,444	10-JUN-99
		GB_HTG2.AC007638	178053	AC007638	Homo sapiens chromosome 17 clone hRPK.515_O_17 map 17, *** SEQUENCING IN PROGRESS ***, 8 unordered pieces.	Homo sapiens	34,821	22-MAY-1999
rx00391	843	GB_EST38:AW01705	613	AW017053	Schistosoma mansoni cDNA clone SMMAS14.5' end, mRNA sequence.	Schistosoma mansoni	40,472	10-SEP-99
		GB_PAT:AR065852	32207	AR065852	Sequence 20 from patent US 5849564.	Unknown.	38,586	29-SEP-99
		GB_VI:AF148805	28559	AF148805	Kaposi's sarcoma-associated herpesvirus ORF 68 gene, partial cds, and ORF 69, kaposin, v-FLIP, v-cyclin, latent nuclear antigen, ORF K14, v-GPCR, putative phosphoribosylformylglycinamide synthase, and LAMP (LAMP) genes, complete cds.	Kaposi's sarcoma-associated herpesvirus	38,509	2-AUG-99
rx00393	1017	GB_BA1.MTY25D10	40838	Z95558	Mycobacterium tuberculosis H37Rv complete genome, segment 28/162.	Mycobacterium tuberculosis	36,308	17-JUN-98
		GB_BA1.MSGY224	40051	AD000004	Mycobacterium tuberculosis sequence from clone y224.	Mycobacterium tuberculosis	39,282	03-DEC-1996
rx00402	623	GB_BA1.MLB1306	7762	Y13803	Mycobacterium leprae cosmid B1306 DNA.	Mycobacterium leprae	39,228	24-JUN-97
		GB_BA2.AF052652	2096	AF052652	Corynebacterium glutamicum homoserine O-acetyltransferase (melA) gene, complete cds.	Corynebacterium glutamicum	99,672	19-MAR-1998
		GB_BA2.AF109162	4514	AF109162	Corynebacterium diphtheriae heme uptake locus, complete sequence.	Corynebacterium diphtheriae	40,830	8-JUN-99
		GB_BA2.AF092918	20758	AF092918	Pseudomonas alcaligenes outer membrane Xcp-secretion system gene cluster.	Pseudomonas alcaligenes	50,161	06-DEC-1998
rx00403	1254	GB_BA2.AF052652	2096	AF052652	Corynebacterium glutamicum homoserine O-acetyltransferase (melA) gene, complete cds.	Corynebacterium glutamicum	99,920	19-MAR-1998
		GB_BA1.MTV016	53662	AL021841	Mycobacterium tuberculosis H37Rv complete genome, segment 143/162.	Mycobacterium tuberculosis	52,898	23-JUN-99
		GB_EST23:AI111288	750	AI111288	SWOVAMCAQ02A05SK Onchocerca volvulus adult male cDNA (SAW98MLW-OvAM) Onchocerca volvulus cDNA clone SWOVAMCAQ02A05 5' mRNA sequence.	Onchocerca volvulus	37,565	31-AUG-98

Table 4 (continued)

αa00405	613	GB_BA1:MTV016	53662	AL021841	Mycobacterium tuberculosis H37Rv complete genome, segment 143/162.	Mycobacterium tuberculosis	57,259	23-Jun-99
		GB_PR4:AC005145	143678	AC005145	Homo sapiens Xp22-166-169 GSHB-523A23 (Genome Systems Human BAC library) complete sequence.	Homo sapiens	34,179	08-DEC-1998
		GB_BA1:MTV016	53662	AL021841	Mycobacterium tuberculosis H37Rv complete genome, segment 143/162.	Mycobacterium tuberculosis	40,169	23-Jun-99
αa00420	1587	GB_BA1:MTY13D12	37085	Z80343	Mycobacterium tuberculosis H37Rv complete genome, segment 156/162.	Mycobacterium tuberculosis	62,031	17-Jun-98
		GB_BA1:MSGY126	37164	AD000012	Mycobacterium tuberculosis sequence from clone y126.	Mycobacterium tuberculosis	61,902	10-DEC-1996
		GB_BA1:MSGB971C	37566	L78821	Mycobacterium leprae cosmid B971 DNA sequence.	Mycobacterium leprae	39,651	15-Jun-96
αa00435	1296	GB_BA1:AFACBBTZ	2760	M68904	Alcaligenes eutrophus chromosomal transketolase (cbbTc) and phosphoglycolate phosphatase (cbbZc) genes, complete cds.	Ralstonia eutropha	38,677	27-Jul-94
		GB_HTG4:AC009541	169583	AC009541	Homo sapiens chromosome 7, *** SEQUENCING IN PROGRESS ***; 25 unordered pieces.	Homo sapiens	36,335	12-OCT-1999
		GB_HTG4:AC009541	169583	AC009541	Homo sapiens chromosome 7, *** SEQUENCING IN PROGRESS ***; 25 unordered pieces.	Homo sapiens	36,335	12-OCT-1999
αa00437	579	GB_PR4:AC005951	155450	AC005951	Homo sapiens chromosome 17, clone hRPK 372_K_20, complete sequence.	Homo sapiens	31,738	18-Nov-98
		GB_BA1:SC2A11	22789	AL031184	Streptomyces coelicolor cosmid 2A11.	Streptomyces coelicolor	43,262	5-Aug-98
		GB_PR4:AC005951	155450	AC005951	Homo sapiens chromosome 17, clone hRPK 372_K_20, complete sequence.	Homo sapiens	37,647	18-Nov-98
αa00439	591	GB_BA1:MTV016	53662	AL021841	Mycobacterium tuberculosis H37Rv complete genome, segment 143/162.	Mycobacterium tuberculosis	37,088	23-Jun-99
		GB_PL2:AF167358	1022	AF167358	Rumex acetosa expansin (EXP3) gene, partial cds.	Rumex acetosa	46,538	17-Aug-99
		GB_HTG3:AC009120	269445	AC009120	Homo sapiens chromosome 16 clone RPCI-11_484E3, *** SEQUENCING IN PROGRESS ***; 34 unordered pieces.	Homo sapiens	43,276	3-Aug-99
αa00440	582	GB_BA2:SKZ86111	7860	Z86111	Streptomyces lividans rpsP, trmD, rplS, sipW, sipX, sipY, sipZ, mutT genes and 4 open reading frames.	Streptomyces lividans	43,080	27-OCT-1999
		GB_BA1:SC2E1	38962	AL023797	Streptomyces coelicolor cosmid 2E1.	Streptomyces coelicolor	42,931	4-Jun-98
		GB_BA1:SC2E1	38962	AL023797	Streptomyces coelicolor cosmid 2E1.	Streptomyces coelicolor	36,702	4-Jun-98
αa00441	1287	GB_PR2:HS173D1	117338	AL031984	Human DNA sequence from clone 173D1 on chromosome 1p36.21-36.33. Contains ESTs, STSs and GSSs, complete sequence.	Homo sapiens	38,027	23-Nov-99
		GB_HTG2:HSDJ719K	267114	AL109931	Homo sapiens chromosome X clone RP4-719K3 map q21.1-21.31, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	34,521	03-DEC-1999
		GB_HTG2:HSDJ719K	267114	AL109931	Homo sapiens chromosome X clone RP4-719K3 map q21.1-21.31, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	34,521	03-DEC-1999
αa00446	987	GB_BA1:SCD78	36224	AL034355	Streptomyces coelicolor cosmid D78.	Streptomyces coelicolor	56,410	26-Nov-98
		GB_HTG4:AC009367	226055	AC009367	Drosophila melanogaster chromosome 3L76A2 clone RPCI88-48B15, *** SEQUENCING IN PROGRESS ***; 44 unordered pieces.	Drosophila melanogaster	34,959	16-OCT-1999
		GB_HTG4:AC009367	226055	AC009367	Drosophila melanogaster chromosome 3L76A2 clone RPCI88-48B15, *** SEQUENCING IN PROGRESS ***; 44 unordered pieces.	Drosophila melanogaster	34,959	16-OCT-1999

Table 4 (continued)

rx000448	1143	GB_PR3:AC003670	88945	AC003670	Homo sapiens 12q13.1 PAC RPC11-130F5 (Roswell Park Cancer Institute Human PAC library) complete sequence.	Homo sapiens	35,682	9-Jun-98
		GB_HTG2:AF029367	148676	AF029367	Homo sapiens chromosome 12 clone RPC1-1 130F5 map 12q13.1, *** SEQUENCING IN PROGRESS ***; 156 unordered pieces.	Homo sapiens	31,373	18-OCT-1997
		GB_HTG2:AF029367	148676	AF029367	Homo sapiens chromosome 12 clone RPC1-1 130F5 map 12q13.1, *** SEQUENCING IN PROGRESS ***; 156 unordered pieces.	Homo sapiens	31,373	18-OCT-1997
rx000450	424	GB_HTG2:AC007824	133361	AC007824	Drosophila melanogaster chromosome 3 clone BACR02L16 (D715) RPC1-98 02.L.16 map 89E-90A strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***; 91 unordered pieces.	Drosophila melanogaster	40,000	2-Aug-99
		GB_HTG2:AC007824	133361	AC007824	Drosophila melanogaster chromosome 3 clone BACR02L16 (D715) RPC1-98 02.L.16 map 89E-90A strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***; 91 unordered pieces.	Drosophila melanogaster	40,000	2-Aug-99
		GB_EST35:A1818057	412	A1818057	wk14a08.x1 NCI_CGAP_Lym12 Homo sapiens cDNA clone IMAGE:2412278 3' similar to gb:Y00764 UBIQUINOL-CYTOCHROME C REDUCTASE 11 KD PROTEIN (HUMAN); mRNA sequence.	Homo sapiens	35,714	24-Aug-99
rx000461	975	GB_BA1:MLCB1779	43254	Z98271	Mycobacterium leprae cosmid B1779.	Mycobacterium leprae	39,308	8-Aug-97
		GB_IN1:DMC86E4	29352	AL021086	Drosophila melanogaster cosmid clone 86E4.	Drosophila melanogaster	37,487	27-Apr-99
rx000465		GB_GSS15:AQ64032	467	AQ640325	927P1-2H3, TP 927P1 Trypanosoma brucei genomic clone 927P1-2H3, genomic survey sequence.	Trypanosoma brucei	38,116	8-Jul-99
rx000487	1692	GB_BA1:BAGUAA	3866	Y10499	B. ammoniagenes guaA gene.	Corynebacterium ammoniagenes	74,259	8-Jan-98
		GB_BA2:U00015	42325	U00015	Mycobacterium leprae cosmid B1620.	Mycobacterium leprae	37,248	01-MAR-1994
		GB_BA1:MTCY78	33818	Z77165	Mycobacterium tuberculosis H37Rv complete genome; segment 145/162.	Mycobacterium tuberculosis	39,725	17-Jun-98
rx000488	1641	GB_BA1:MTCY78	33818	Z77165	Mycobacterium tuberculosis H37Rv complete genome; segment 145/162.	Mycobacterium tuberculosis	39,451	17-Jun-98
		GB_BA2:U00015	42325	U00015	Mycobacterium leprae cosmid B1620.	Mycobacterium leprae	39,178	01-MAR-1994
rx000489	1245	GB_BA1:SCAJ10601	4692	AJ010601	Streptomyces coelicolor A3(2) DNA for whiD and whiK loci.	Streptomyces coelicolor	60,835	17-Sep-98
		GB_BA2:U00015	42325	U00015	Mycobacterium leprae cosmid B1620.	Mycobacterium leprae	38,041	01-MAR-1994
		GB_HTG2:HS225E12	126464	AL031772	Homo sapiens chromosome 6 clone RP1-225E12 map q24, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	36,756	03-DEC-1999
		GB_HTG2:HS225E12	126464	AL031772	Homo sapiens chromosome 6 clone RP1-225E12 map q24, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	36,756	03-DEC-1999
rx000533	1155	GB_BA1:CGLYS	2803	X57226	C. glutamicum lysC-alpha, lysC-beta and asd genes for aspartokinase-alpha and -beta subunits, and aspartate beta semialdehyde dehydrogenase, respectively (EC 2.7.2.4; EC 1.2.1.11).	Corynebacterium glutamicum	99,913	17-Feb-97

Table 4 (continued)

Table 4 (continued)

	GB_PAT:AR016483	2104	AR016483	Sequence 1 from patent US 5776740.		Unknown.	99,368	05-DEC-1998
	EM_PAT:E11273	2104	E11273	DNA encoding serine hydroxymethyl transferase.		Corynebacterium glutamicum	99,368	08-OCT-1997 (Rel. 52, Created) 24-Jun-98
rx00581	GB_PAT:E12594	2104	E12594	DNA encoding serine hydroxymethyltransferase from <i>Brevibacterium flavum</i> .		Corynebacterium glutamicum	37,071	08-OCT-1997 (Rel. 52, Created) 05-DEC-1998
	EM_PAT:E11273	2104	E11273	DNA encoding serine hydroxymethyl transferase.		Corynebacterium glutamicum	37,071	08-OCT-1997 (Rel. 52, Created) 05-DEC-1998
	GB_PAT:AR016483	2104	AR016483	Sequence 1 from patent US 5776740.		Unknown.	37,071	05-DEC-1998
rx00584	GB_BA1:CORAHPS	2570	L07603	Corynebacterium glutamicum 3-deoxy-D-arabinoheptulosonate-7-phosphate synthase gene, complete cds.		Corynebacterium glutamicum	98,236	26-Apr-93
	GB_BA1:AOPCZA361	37941	AJ233998	Amycolatopsis orientalis cosmid PCZA361.		Amycolatopsis orientalis	54,553	29-MAR-1999
rx00618	GB_BA1:D90714	14358	D90714	<i>Escherichia coli</i> genomic DNA. (16.8 - 17.1 min).		<i>Escherichia coli</i>	53,312	7-Feb-99
	GB_EST19:AA802737	280	AA802737	GM06236.5prime GM <i>Drosophila melanogaster</i> ovary BlueScript <i>Drosophila melanogaster</i> cDNA clone GM06236.5prime, mRNA sequence.		<i>Drosophila melanogaster</i>	39,928	25-Nov-98
	GB_EST28:AI534381	581	AI534381	SD07186.5prime SD <i>Drosophila melanogaster</i> Schneider L2 cell culture pOT2 <i>Drosophila melanogaster</i> cDNA clone SD07186.5prime similar to X89858: Anl FBgn0011558 PID:g927407 SPTREMBL:Q24240, mRNA sequence.		<i>Drosophila melanogaster</i>	41,136	18-MAR-1999
rx00619	GB_IN1:DMANILLIN	4029	X89858	<i>D. melanogaster</i> mRNA for anillin protein.		<i>Drosophila melanogaster</i>	34,398	8-Nov-95
	GB_BA1:MTCY369	36850	Z80226	<i>Mycobacterium tuberculosis</i> H37Rv complete genome; segment 36/162.		<i>Mycobacterium tuberculosis</i>	62,776	17-Jun-98
	GB_BA1:MLCB5	38109	Z95151	<i>Mycobacterium leprae</i> cosmid B5.		<i>Mycobacterium leprae</i>	61,831	24-Jun-97
	GB_PAT:A60305	1845	A60305	Sequence 5 from Patent WO9708323.		unidentified	61,785	06-MAR-1998
rx00620	GB_PL2:AF063247	1450	AF063247	<i>Pneumocystis carinii</i> f. sp. <i>ratti</i> endonase mRNA, complete cds.		<i>Pneumocystis carinii</i> f. sp. <i>ratti</i>	41,060	5-Jan-99
	GB_BA1:STMAPP	2069	M91546	<i>Streptomyces lividans</i> aminopeptidase P (PepP) gene, complete cds.		<i>Streptomyces lividans</i>	37,126	12-Jun-93
	GB_HTG3:AC008763	214575	AC008763	<i>Homo sapiens</i> chromosome 19 clone CITB-E1_3214H19, *** SEQUENCING IN PROGRESS ***, 21 unordered pieces.		<i>Homo sapiens</i>	40,020	3-Aug-99
rx00624	GB_IN1:CEY41E3	150641	Z95559	<i>Caenorhabditis elegans</i> cosmid Y41E3, complete sequence.		<i>Caenorhabditis elegans</i>	36,986	2-Sep-99
	GB_EST13:AA362167	372	AA362167	EST71561 Macrophage 1 <i>Homo sapiens</i> cDNA 5' end, mRNA sequence.		<i>Homo sapiens</i>	38,378	21-Apr-97
rx00626	GB_IN1:CEY41E3	150641	Z95559	<i>Caenorhabditis elegans</i> cosmid Y41E3, complete sequence.		<i>Caenorhabditis elegans</i>	37,694	2-Sep-99
	GB_BA1:MTCY369	36850	Z80226	<i>Mycobacterium tuberculosis</i> H37Rv complete genome; segment 36/162.		<i>Mycobacterium tuberculosis</i>	57,971	17-Jun-98
	GB_BA1:MLCB5	38109	Z95151	<i>Mycobacterium leprae</i> cosmid B5.		<i>Mycobacterium leprae</i>	58,806	24-Jun-97
	GB_BA1:MLU15187	36138	U15187	<i>Mycobacterium leprae</i> cosmid L296.		<i>Mycobacterium leprae</i>	38,007	09-MAR-1995

Table 4 (continued)

rx00632	795	GB_BA1:BRLBIOAD	2272	D14083	Brevibacterium flavum genes for 7,8-diaminopelargonic acid aminotransferase and dethiobiotin synthetase, complete cds.	Corynebacterium glutamicum	97,358	3-Feb-99
		GB_PAT:E04041	675	E04041	DNA sequence coding for dethiobiotin synthetase.	Corynebacterium glutamicum	98,074	29-Sep-97
		GB_PAT:E04040	1272	E04040	DNA sequence coding for diamino pelargonic acid aminotransferase.	Corynebacterium glutamicum	93,814	29-Sep-97
rx00633	1392	GB_BA1:BRLBIOAD	2272	D14083	Brevibacterium flavum genes for 7,8-diaminopelargonic acid aminotransferase and dethiobiotin synthetase, complete cds.	Corynebacterium glutamicum	95,690	3-Feb-99
		GB_PAT:E04040	1272	E04040	DNA sequence coding for diamino pelargonic acid aminotransferase.	Corynebacterium glutamicum	95,755	29-Sep-97
rx00668	566	GB_BA2:EHU38519	1290	U38519	Erwinia herbicola adenosylmethionine-8-amino-7-oxononanoate transaminase (bioA) gene, complete cds.	Erwinia herbicola	55,564	4-Nov-96
		GB_BA1:MTV041	28826	AL021958	Mycobacterium tuberculosis H37Rv complete genome; segment 35/162.	Mycobacterium tuberculosis	60,030	17-Jun-98
		GB_BA1:BRLSECY	1516	D14162	Brevibacterium flavum gene for SecY protein (complete cds) and gene or adenylate kinase (partial cds).	Corynebacterium glutamicum	99,563	3-Feb-99
		GB_BA2:MBU77912	7163	U77912	Mycobacterium bovis MBE50a gene, partial cds; and MBE50b, MBE50c, preprotein translocase SecY subunit (secY), adenylate kinase (adk), methionine aminopeptidase (map), RNA polymerase ECF sigma factor (sigE50), MBE50d, and MBE50e genes, complete cds.	Mycobacterium bovis	60,030	27-Jan-99
rx00708	930	GB_BA2:AF157493	25454	AF157493	Zymomonas mobilis ZM4 fosmid clone 42D7, complete sequence.	Zymomonas mobilis	39,116	5-Jul-99
		GB_PAT:I00836	1853	I00836	Sequence 1 from Patent US 4758514.	Unknown.	47,419	21-MAY-1993
rx00717	1083	GB_PAT:E00311	1853	E00311	DNA coding of 2,5-diketogluconic acid reductase.	unidentified	47,419	29-Sep-97
		GB_PAT:I78753	1187	I78753	Sequence 9 from patent US 5693781.	Unknown.	37,814	3-Apr-98
		GB_PAT:I92042	1187	I92042	Sequence 9 from patent US 5726299.	Unknown.	37,814	01-DEC-1998
rx00718	831	GB_BA1:MTCI125	37432	Z98268	Mycobacterium tuberculosis H37Rv complete genome; segment 76/162.	Mycobacterium tuberculosis	50,647	17-Jun-98
		GB_BA1:MTCI125	37432	Z98268	Mycobacterium tuberculosis H37Rv complete genome; segment 76/162.	Mycobacterium tuberculosis	55,228	17-Jun-98
		GB_BA1:MTCI125	37432	Z98268	Mycobacterium tuberculosis H37Rv complete genome; segment 76/162.	Mycobacterium tuberculosis	40,300	17-Jun-98
rx00727	1035	GB_GSS12:AQ42075	671	AQ42075	RPCL-11-168G18 TJ RPCL-11 Homo sapiens genomic clone RPCL-11-168G18, genomic survey sequence.	Homo sapiens	35,750	23-MAR-1999
		GB_HTG3:AC008332	118545	AC008332	Drosophila melanogaster chromosome 2 clone BACR48D10 (D867) RPCL-98 48 D.10 map 34A-34A strain y; cn bw sp. *** SEQUENCING IN PROGRESS	Drosophila melanogaster	40,634	6-Aug-99
		GB_HTG3:AC008332	118545	AC008332	Drosophila melanogaster chromosome 2 clone BACR48D10 (D867) RPCL-98 48 D.10 map 34A-34A strain y; cn bw sp. *** SEQUENCING IN PROGRESS***, 78 unordered pieces.	Drosophila melanogaster	40,634	6-Aug-99

Table 4 (continued)

GB_HTG3:AC008332	118545	AC008332	Drosophila melanogaster chromosome 2 clone BACR48D10 (D867) RPCI-98 48.D.10 map 34A-34A strain y; cn bw sp. *** SEQUENCING IN PROGRESS***, 78 unordered pieces.	33,888	6-Aug-99
GB_HTG2:AC006789	83823	AC006789	Caenorhabditis elegans clone Y49F6, *** SEQUENCING IN PROGRESS***, 2 unordered pieces.	36,737	25-Feb-99
GB_HTG2:AC006789	83823	AC006789	Caenorhabditis elegans clone Y49F6, *** SEQUENCING IN PROGRESS***, 2 unordered pieces.	36,737	25-Feb-99
GB_BA1:D90810	20476	D90810	E. coli genomic DNA, Kohara clone #319(37.4-37.8 min.).	36,526	29-MAY-1997
GB_BA1:MTV043	68848	AL022004	Mycobacterium tuberculosis H37Rv complete genome; segment 40/162.	66,193	24-Jun-99
GB_BA1:MLU15182	40123	U15182	Mycobacterium leprae cosmid B2266.	61,443	09-MAR-1995
GB_BA2:SCD25	41622	AL118514	Streptomyces coelicolor cosmid D25.	59,938	21-Sep-99
GB_HTG1:CER08A5	51920	Z82281	Caenorhabditis elegans chromosome V clone R08A5, *** SEQUENCING IN PROGRESS***, in unordered pieces.	64,896	14-OCT-1998
GB_HTG1:CER08A5	51920	Z82281	Caenorhabditis elegans chromosome V clone R08A5, *** SEQUENCING IN PROGRESS***, in unordered pieces.	64,896	14-OCT-1998
GB_PL2:AF078693	1492	AF078693	Chlamydomonas reinhardtii putative O-acetylserine(thiol)lyase precursor (Crcys-1A) mRNA, nuclear gene encoding organellar protein, complete cds.	57,970	3-Nov-99
GB_BA1:MTCY98	31225	Z83860	Mycobacterium tuberculosis H37Rv complete genome; segment 103/162.	54,410	17-Jun-98
GB_BA1:AVINIFREG	7099	M60090	Azotobacter chroococcum nifU, nifS, nifV, nifP, nifW, nifZ and nifM genes, complete cds.	51,729	26-Apr-93
GB_BA2:AF001780	6701	AF001780	Cyanothece PCC 8801 NifP (nifP), nitrogenase (nifB), FdxN (fdxN), NifS (nifS) and NifU (nifU) genes, complete cds, and NifH (nifH) gene, partial cds.	36,309	08-MAR-1999
GB_EST1:Z30506	329	Z30506	ATTS2430 AC16H Arabidopsis thaliana cDNA clone TAI306 3', mRNA sequence.	44,308	11-MAR-1994
GB_PL2:AC006258	110469	AC006258	Arabidopsis thaliana BAC F18G18 from chromosome V near 60.5 cM, complete sequence.	35,571	28-DEC-1998
GB_EST37:A1998439	455	A1998439	701545695 A. thaliana, Columbia Col-0, rosette-2 Arabidopsis thaliana cDNA clone 701545695, mRNA sequence.	36,044	8-Sep-99
GB_BA1:BLDAPAB	3572	Z21502	B. lactofermentum dapA and dapB genes for dihydrodipicolinate synthase and dihydrodipicolinate reductase.	99,539	16-Aug-93
GB_PAT:E16749	2001	E16749	gDNA encoding dihydrodipicolinate synthase (DDPS).	99,539	28-Jul-99
GB_PAT:E14520	2001	E14520	DNA encoding Brevibacterium dihydrodipicolinic acid synthase.	99,539	28-Jul-99
GB_BA1:BLDAPAB	3572	Z21502	B. lactofermentum dapA and dapB genes for dihydrodipicolinate synthase and dihydrodipicolinate reductase.	99,885	16-Aug-93
GB_BA1:CGDAPB	1902	X67737	C. glutamicum dapB gene for dihydrodipicolinate reductase.	100,000	1-Apr-93

Table 4 (continued)

rx000865	1026	GB_PAT:E14520	2001	E14520	DNA encoding Brevibacterium dihydrodipicolinic acid synthase.	Corynebacterium glutamicum	100,000	28-Jul-99
		GB_BA1:BLDAPAB	3572	Z21502	B.lactofermentum dapA and dapB genes for dihydrodipicolinate synthase and dihydrodipicolinate reductase.	Corynebacterium glutamicum	100,000	16-Aug-93
		GB_PAT:E16752	1411	E16752	gDNA encoding dihydrodipicolinate reductase (DDPR).	Corynebacterium glutamicum	99,805	28-Jul-99
rx000867	650	GB_PAT:AR038113	1411	AR038113	Sequence 18 from patent US 5804414.	Unknown.	99,805	29-Sep-99
		GB_BA1:MTV002	56414	AL008967	Mycobacterium tuberculosis H37Rv complete genome; segment 122/162.	Mycobacterium tuberculosis	39,179	17-Jun-98
		GB_BA1:MLCB22	40281	Z98741	Mycobacterium leprae cosmid B22.	Mycobacterium leprae	39,482	22-Aug-97
		GB_BA1:SAU19858	2838	U19858	Streptomyces antibioticus guanosine pentaphosphate synthetase (gpsI) gene, complete cds.	Streptomyces antibioticus	69,706	25-OCT-1996
rx000873	779	GB_BA1:SCO001206	9184	AJ001206	Streptomyces coelicolor A3(2), glycogen metabolism cluster II.	Streptomyces coelicolor	63,415	29-MAR-1999
		GB_BA1:SCO001205	9589	AJ001205	Streptomyces coelicolor A3(2) glycogen metabolism cluster.	Streptomyces coelicolor	61,617	29-MAR-1999
rx000884	1263	GB_BA1:D78198	2304	D78198	Pimeleobacter sp. DNA for trehalose synthase, complete cds.	Pimeleobacter sp.	60,594	5-Feb-99
		GB_BA1:MTCY253	41230	Z81368	Mycobacterium tuberculosis H37Rv complete genome; segment 106/162.	Mycobacterium tuberculosis	37,785	17-Jun-98
		GB_BA1:MSGY222	41156	AD000010	Mycobacterium tuberculosis sequence from clone y222.	Mycobacterium tuberculosis	38,006	03-DEC-1996
		GB_GSS15:AQ65460	468	AQ654600	Sheared DNA-1014, TF Sheared DNA Trypanosoma brucei genomic clone 0	Trypanosoma brucei	33,974	22-Jun-99
rx000891	1102	GB_BA1:MTCI418B	11700	Z96071	Sheared DNA-1014, genomic survey sequence.	Mycobacterium tuberculosis	63,297	18-Jun-98
		GB_BA1:SCO001206	9184	AJ001206	Mycobacterium tuberculosis H37Rv complete genome; segment 7/162.	Mycobacterium tuberculosis	61,965	29-MAR-1999
		GB_BA1:SCO001205	9589	AJ001205	Streptomyces coelicolor A3(2), glycogen metabolism cluster II.	Streptomyces coelicolor	61,727	29-MAR-1999
rx000952	963	EM_PAT:E10963	3118	E10963	gDNA encoding tryptophan synthase.	Corynebacterium glutamicum	99,688	08-OCT-1997 (Rel. 52, Created)
		GB_BA1:BLTRP	7725	X04960	Brevibacterium lactofermentum tryptophan operon.	Corynebacterium glutamicum	98,847	10-Feb-99
rx000954	644	GB_PAT:E01688	7725	E01688	Genomic DNA of trp operon of prepibacterium latopheimentam.	unidentified	98,428	29-Sep-97
		GB_PAT:E01375	7726	E01375	DNA sequence of tryptophan operon.	Corynebacterium glutamicum	98,758	29-Sep-97
		GB_PAT:E01688	7725	E01688	Genomic DNA of trp operon of prepibacterium latopheimentam.	unidentified	98,758	29-Sep-97
		GB_BA1:BLTRP	7725	X04960	Brevibacterium lactofermentum tryptophan operon.	Corynebacterium glutamicum	98,758	10-Feb-99
rx000955	1545	GB_PAT:E01375	7726	E01375	DNA sequence of tryptophan operon.	Corynebacterium glutamicum	98,372	29-Sep-97

Table 4 (continued)

Table 4 (continued)

rx000997	705	GB_BA2:CGU31225	1817	U3_225	Corynebacterium glutamicum complete cds.	Corynebacterium glutamicum	40,841	2-Aug-96
		GB_HTG1:CEY39C12	282838	AL009026	Caenorhabditis elegans chromosome IV clone Y39C12, *** SEQUENCING IN PROGRESS ***	Caenorhabditis elegans	36,416	26-OCT-1999
		GB_IN1:CEB0001	39416	Z69634	Caenorhabditis elegans cosmid B0001, complete sequence.	Caenorhabditis elegans	36,416	2-Sep-99
rx01019	1110	GB_HTG2:AC005052	144734	AC005052	Homo sapiens clone RG038K21, *** SEQUENCING IN PROGRESS ***	Homo sapiens	39,172	12-Jun-98
		GB_HTG2:AC005052	144734	AC005052	Homo sapiens clone RG038K21, *** SEQUENCING IN PROGRESS ***	Homo sapiens	39,172	12-Jun-98
		GB_GSS9:AQ171808	512	AQ171808	HS_3179_A1_G03_T7 CIT Approved Human Genomic Sperm Library D Homo sapiens genomic clone Plate=3179 Col=5 Row=M, genomic survey sequence.	Homo sapiens	34,661	17-OCT-1998
rx01026	1782	GB_BA1:SC1C2	42210	AL031124	Streptomyces coelicolor cosmid 1C2.	Streptomyces coelicolor	68,275	15-Jan-99
		GB_BA1:ATLEUCD	2982	X84647	A. teichomyceticus leuC and leuD genes.	Actinoplanes teichomyceticus	65,935	04-OCT-1995
		GB_BA1:MTV012	70287	AL021287	Mycobacterium tuberculosis H37Rv complete genome; segment 132/162.	Mycobacterium tuberculosis	40,454	23-Jun-99
rx01027	1131	GB_BA1:MLCB637	44882	Z99263	Mycobacterium leprae cosmid B637.	Mycobacterium leprae	38,636	17-Sep-97
		GB_BA1:MTCY349	43523	Z83018	Mycobacterium tuberculosis H37Rv complete genome; segment 131/162.	Mycobacterium tuberculosis	51,989	17-Jun-98
rx01073	954	GB_BA1:SPUNGUMUT X	1172	Z21702	S. pneumoniae ung gene and muX genes encoding uracil-DNA glycosylase and 8-oxodGTP nucleoside triphosphatase.	Streptococcus pneumoniae	38,088	15-Jun-94
		GB_BA1:BACOUTB	1004	M15811	Bacillus subtilis outB gene encoding a sporulation protein, complete cds.	Bacillus subtilis	53,723	26-Apr-93
		GB_PR4:AC007938	167237	AC007938	Homo sapiens clone UWGC-djs201 from 7q31, complete sequence.	Homo sapiens	34,322	1-Jul-99
		GB_PL2:ATAC006282	92577	AC006282	Arabidopsis thaliana chromosome II BAC F13K3 genomic sequence, complete sequence.	Arabidopsis thaliana	36,181	13-MAR-1999
rx01079	2226	GB_BA2:AF112535	4363	AF112535	Corynebacterium glutamicum putative glutaredoxin NrdH (nrdH), NrdI (nrdI), and ribonucleotide reductase alpha-chain (nrdE) genes, complete cds.	Corynebacterium glutamicum	99,820	5-Aug-99
		GB_BA1:CANRDFGE N	6054	Y09572	Corynebacterium ammoniagenes nrdH, nrdI, nrdE, nrdF genes.	Corynebacterium ammoniagenes	75,966	18-Apr-98
		GB_BA1:MTV012	70287	AL021287	Mycobacterium tuberculosis H37Rv complete genome; segment 132/162.	Mycobacterium tuberculosis	38,296	23-Jun-99
rx01080	567	GB_BA2:AF112535	4363	AF112535	Corynebacterium glutamicum putative glutaredoxin NrdH (nrdH), NrdI (nrdI), and ribonucleotide reductase alpha-chain (nrdE) genes, complete cds.	Corynebacterium glutamicum	100,000	5-Aug-99
		GB_BA1:CANRDFGE N	6054	Y09572	Corynebacterium ammoniagenes nrdH, nrdI, nrdE, nrdF genes.	Corynebacterium ammoniagenes	65,511	18-Apr-98
		GB_BA1:STNRD	4894	X73226	S. typhimurium nrdEF operon.	Salmonella typhimurium	52,477	03-MAR-1997
rx01087	999	GB_IN2:AF063412	1093	AF063412	Limnadia lenticularis elongation factor 1-alpha mRNA, partial cds.	Limnadia lenticularis	43,750	29-MAR-1999
		GB_PR3:HS24M15	134539	Z94055	Human DNA sequence from PAC 24M15 on chromosome 1. Contains tenascin-R (restrictin), EST.	Homo sapiens	37,475	23-Nov-99
		GB_IN2:ARU85702	1240	U85702	Anathix ralla elongation factor-1 alpha (EF-1a) gene, partial cds.	Anathix ralla	37,319	16-Jul-97

Table 4 (continued)

rx01095	857	GB_BA1.MTCY01B2	35938	Z95554	Mycobacterium tuberculosis H37Rv complete genome; segment 72/162.	Mycobacterium tuberculosis	43,243	17-Jun-98
		GB_HTG5.AC011632	175917	AC011632	Homo sapiens clone RP11-3N13, WORKING DRAFT SEQUENCE, 9 unordered pieces.	Homo sapiens	36,471	19-Nov-99
		GB_HTG5.AC011632	175917	AC011632	Homo sapiens clone RP11-3N13, WORKING DRAFT SEQUENCE, 9 unordered pieces.	Homo sapiens	36,836	19-Nov-99
rx01097	477	GB_BA2.AF030405	774	AF030405	Corynebacterium glutamicum cyclase (hisF) gene, complete cds.	Corynebacterium glutamicum	100,000	13-Nov-97
		GB_BA2.AF030405	774	AF030405	Corynebacterium glutamicum cyclase (hisF) gene, complete cds.	Corynebacterium glutamicum	41,206	13-Nov-97
rx01098	897	GB_BA2.AF030405	774	AF030405	Corynebacterium glutamicum cyclase (hisF) gene, complete cds.	Corynebacterium glutamicum	97,933	13-Nov-97
		GB_BA1.MSGY223	42061	AD000019	Mycobacterium tuberculosis sequence from clone y223.	Mycobacterium tuberculosis	40,972	10-DEC-1996
		GB_BA1.MLCB1610	40055	AL049913	Mycobacterium leprae cosmid B1610.	Mycobacterium leprae	61,366	27-Aug-99
rx01100	861	GB_BA2.AF051846	738	AF051846	Corynebacterium glutamicum phosphoribosylformimino-5-amino-1-phosphoribosyl-4-imidazolecarboxamide isomerase (hisA) gene, complete cds.	Corynebacterium glutamicum	97,154	12-MAR-1998
		GB_BA2.AF060558	636	AF060558	Corynebacterium glutamicum glutamine amidotransferase (hisH) gene, complete cds.	Corynebacterium glutamicum	95,455	29-Apr-98
		GB_HTG1.HSDJ140A	221755	AL109917	Homo sapiens chromosome 1 clone RP1-140A9, *** SEQUENCING IN PROGRESS ***, in unordered pieces.	Homo sapiens	30,523	23-Nov-99
rx01101	756	GB_BA2.AF060558	636	AF060558	Corynebacterium glutamicum glutamine amidotransferase (hisH) gene, complete cds.	Corynebacterium glutamicum	94,462	29-Apr-98
		GB_BA1.SC4G6	36917	AL096884	Streptomyces coelicolor cosmid 4G6.	Streptomyces coelicolor A3(2)	38,378	23-Jul-99
		GB_BA1.STMHISOPA	3981	M31628	S. coelicolor histidine biosynthesis operon encoding hisD, partial cds., and hisC, hisB, hisH, and hisA genes, complete cds.	Streptomyces coelicolor	60,053	26-Apr-93
rx01104	729	GB_BA1.STMHISOPA	3981	M31628	S. coelicolor histidine biosynthesis operon encoding hisD, partial cds., and hisC, hisB, hisH, and hisA genes, complete cds.	Streptomyces coelicolor	58,333	26-Apr-93
		GB_BA1.SC4G6	36917	AL096884	Streptomyces coelicolor cosmid 4G6.	Streptomyces coelicolor A3(2)	39,045	23-Jul-99
		GB_BA1.MTCY336	32437	Z95586	Mycobacterium tuberculosis H37Rv complete genome; segment 70/162.	Mycobacterium tuberculosis	60,364	24-Jun-99
rx01105	1221	GB_BA1.MTCY336	32437	Z95586	Mycobacterium tuberculosis H37Rv complete genome; segment 70/162.	Mycobacterium tuberculosis	60,931	24-Jun-99
		GB_BA1.MSGY223	42061	AD000019	Mycobacterium tuberculosis sequence from clone y223.	Mycobacterium tuberculosis	36,851	10-DEC-1996
		GB_BA1.MLCB1610	40055	AL049913	Mycobacterium leprae cosmid B1610.	Mycobacterium leprae	60,902	27-Aug-99
rx01106	1449	GB_BA1.MSGY223	42061	AD000019	Mycobacterium tuberculosis sequence from clone y223.	Mycobacterium tuberculosis	37,233	10-DEC-1996

M. smegmatis genes *hisD* and *hisC* for histidinol dehydrogenase and histidinol-Mycobacterium smegmatis 60,111 phosphate aminotransferase, respectively.

[illegible]

Table 4 (continued)

αa01321	1044	GB_GSS14:AQ51884_3	441	AQ518843	HS_5106_A1_D10_SP6E RPC1-11 Human Male BAC Library Homo sapiens genomic clone Plate=682 Col=19 Row=G, genomic survey sequence.	Homo sapiens	41,121	05-MAY-1999
		GB_HTG2:AC007473	194859	AC007473	Drosophila melanogaster chromosome 2 clone BACR38D12 (D590) RPC1-98 38.D 12 map 48A-48B strain y; cn bw sp, *** SEQUENCING IN PROGRESS	Drosophila melanogaster	40,534	2-AUG-99
		GB_HTG4:AC011696	115847	AC011696	***, 60 unordered pieces. Drosophila melanogaster chromosome 2 clone BACR35F01 (D1156) RPC1-98 35.F 1 map 48A-48C strain y; cn bw sp, *** SEQUENCING IN PROGRESS	Drosophila melanogaster	38,290	26-OCT-1999
αa01352	706	GB_PL2:ATAC005167	83260	AC005167	***, 108 unordered pieces. Arabidopsis thaliana chromosome II BAC F12A24 genomic sequence, complete sequence.	Arabidopsis thaliana	34,311	15-OCT-1998
		GB_PL2:ATAC005825	97380	AC005825	Arabidopsis thaliana chromosome II BAC T24121 genomic sequence, complete sequence.	Arabidopsis thaliana	34,311	12-APR-99
		GB_HTG3:AC011150	127222	AC011150	Homo sapiens clone 4_K_17, LOW-PASS SEQUENCE SAMPLING.	Homo sapiens	37,722	01-OCT-1999
αa01360	259	GB_EST32:A1725583	728	A1725583	BNLGH112371 Six-day Cotton fiber Gossypium hirsutum cDNA 5' similar to (U86081) root hair defective 3 [Arabidopsis thaliana], mRNA sequence.	Gossypium hirsutum	38,492	11-JUN-99
		GB_PR2:HS227P17	82951	Z81007	Human DNA sequence from PAC 227P17, between markers DXS6791 and DXS8038 on chromosome X contains CpG island, EST.	Homo sapiens	39,738	23-NOV-99
		GB_EST34:AV171099	173	AV171099	AV171099 Mus musculus head C57BL/6J 14, 17 day embryo Mus musculus cDNA clone 3200002M11, mRNA sequence.	Mus musculus	46,237	6-JUL-99
αa01361	629	GB_RO:AB008915S1	530	AB008915	Mus musculus mGpi1 gene, exon 1.	Mus musculus	45,574	28-SEP-99
		GB_EST22:A1050532	293	A1050532	uc83d10.y1 Sugano mouse kidney mKia Mus musculus cDNA clone IMAGE:1432243 5' similar to TR:O35120 O35120 MGP11P. ., mRNA sequence.	Mus musculus	44,097	9-JUL-98
αa01381	944	GB_RO:AB008895	3062	AB008895	Mus musculus mRNA for mGpi1p, complete cds.	Mus musculus	41,316	23-NOV-97
		GB_PL1:AB005237	87835	AB005237	Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MJJ3, complete sequence.	Arabidopsis thaliana	36,606	20-NOV-99
		GB_GSS5:AQ766840	491	AQ766840	HS_2026_A2_C09_T7C CIT Approved Human Genomic Sperm Library D Homo sapiens genomic clone Plate=2026 Col=18 Row=E, genomic survey sequence.	Homo sapiens	37,916	28-JUL-99
αa01393	993	GB_BA1:MTV043	68848	AL022004	Mycobacterium tuberculosis H37Rv complete genome, segment 40/162.	Mycobacterium tuberculosis	37,419	24-JUN-99
		GB_BA1:CGLYSEG	2374	X96471	C. glutamicum lysE and lysG genes.	Corynebacterium glutamicum	34,831	24-FEB-97
		GB_BA1:SC5A7	40337	AL031107	Streptomyces coelicolor cosmid 5A7	Streptomyces coelicolor	35,138	27-JUL-98
		GB_PR3:AC004054	112184	AC004054	Homo sapiens chromosome 4 clone B220G8 map 4q21, complete sequence.	Homo sapiens	37,277	9-JUL-98
αa01394	822	GB_BA1:CGLYSEG	2374	X96471	C. glutamicum lysE and lysG genes.	Corynebacterium glutamicum	100,000	24-FEB-97
		GB_GSS5:AQ769223	500	AQ769223	HS_3155_B2_G10_T7C CIT Approved Human Genomic Sperm Library D Homo sapiens genomic clone Plate=3155 Col=20 Row=N, genomic survey sequence.	Homo sapiens	38,400	28-JUL-99

Table 4 (continued)

	GB_BA1:CGLYSEG	2374	X96471	C. glutamicum lysE and lysG genes.	Corynebacterium glutamicum	33,665	24-Feb-97
rx01416	630	GB_BA1:SC3C3	31382	Streptomyces coelicolor cosmid 3C3.	Streptomyces coelicolor	62,726	10-Aug-98
		GB_BA1:MLCB22	40281	Mycobacterium leprae cosmid B22.	Mycobacterium leprae	39,159	22-Aug-97
		GB_BA1:MTV002	56414	Mycobacterium tuberculosis H37Rv complete genome; segment 122/162.	Mycobacterium tuberculosis	37,340	17-Jun-98
rx01442	1347	GB_BA1:D90827	18886	E. coli genomic DNA, Kohara clone #336(41.2-41.6 min.).	Escherichia coli	58,517	21-MAR-1997
		GB_BA1:D90828	14590	E. coli genomic DNA, Kohara clone #336gap(41.6-41.9 min.).	Escherichia coli	56,151	21-MAR-1997
rx01446	1413	GB_BA2:AE000279	10855	Escherichia coli K-12 MG1655 section 169 of 400 of the complete genome.	Escherichia coli	56,021	12-Nov-98
		GB_BA1:SCH10	39524	Streptomyces coelicolor cosmid H10.	Streptomyces coelicolor	39,037	04-MAY-1999
		GB_BA1:MTY13E10	35019	Mycobacterium tuberculosis H37Rv complete genome; segment 18/162.	Mycobacterium tuberculosis	40,130	17-Jun-98
rx01483	1395	GB_BA1:MLCB4	36310	Mycobacterium leprae cosmid B4.	Mycobacterium leprae	37,752	27-Aug-99
		GB_BA1:MTY98	31225	Mycobacterium tuberculosis H37Rv complete genome; segment 103/162.	Mycobacterium tuberculosis	39,057	17-Jun-98
		GB_BA1:MSGB1229C	30670	Mycobacterium leprae cosmid B1229 DNA sequence.	Mycobacterium leprae	54,382	15-Jun-96
rx01486	757	GB_BA2:AF027507	5168	Mycobacterium smegmatis dGTPase (dgt), and primase (dnaG) genes, complete cds; tRNA-Asn gene, complete sequence.	Mycobacterium smegmatis	52,941	16-Jan-98
		GB_BA1:MTV002	56414	Mycobacterium tuberculosis H37Rv complete genome; segment 122/162.	Mycobacterium tuberculosis	40,941	17-Jun-98
rx01489	1146	GB_BA1:MLCB22	40281	Mycobacterium leprae cosmid B22.	Mycobacterium leprae	38,451	22-Aug-97
		GB_BA1:SC3C3	31382	Streptomyces coelicolor cosmid 3C3.	Streptomyces coelicolor	61,194	10-Aug-98
		GB_BA1:CORFADS	1547	Corynebacterium ammoniagenes gene for FAD synthetase, complete cds.	Corynebacterium ammoniagenes	58,021	8-Feb-99
		GB_BA1:MLCB22	40281	Mycobacterium leprae cosmid B22.	Mycobacterium leprae	38,414	22-Aug-97
rx01491	774	GB_BA1:SC10A7	39739	Streptomyces coelicolor cosmid 10A7.	Streptomyces coelicolor	36,930	9-Jun-99
		GB_BA1:MTV002	56414	Mycobacterium tuberculosis H37Rv complete genome; segment 122/162.	Mycobacterium tuberculosis	37,062	17-Jun-98
		GB_EST13:AA356956	255	EST65614 Jurkat T-cells III Homo sapiens cDNA 5' end, mRNA sequence.	Homo sapiens	37,647	21-Apr-97
		GB_OV:OMDNAPROI	7327	O. mossambicus prolactin I gene.	Tilapia mossambica	38,289	19-OCT-1995
rx01508	1662	GB_IN1:CEF28C12	14653	Caenorhabditis elegans cosmid F28C12, complete sequence.	Caenorhabditis elegans	37,984	23-Nov-98
		GB_IN1:CEF28C12	14653	Caenorhabditis elegans cosmid F28C12, complete sequence.	Caenorhabditis elegans	38,469	23-Nov-98
rx01512	723	GB_BA1:SCE9	37730	Streptomyces coelicolor cosmid E9.	Streptomyces coelicolor	39,021	19-MAY-1999
		GB_BA1:MAU88875	840	Mycobacterium avium hypoxanthine-guanine phosphoribosyl transferase gene, complete cds.	Mycobacterium avium	57,521	05-MAR-1997

Table 4 (continued)

αa01514	711	GB_BA1:MTY15C10	33050	Z95436	Mycobacterium tuberculosis H37Rv complete genome; segment 154/162.	Mycobacterium tuberculosis	40,086	17-Jun-98
		GB_BA1:MTY7H7B	24244	Z95557	Mycobacterium tuberculosis H37Rv complete genome; segment 153/162.	Mycobacterium tuberculosis	43,343	18-Jun-98
		GB_BA1:MLCB2548	38916	AL023093	Mycobacterium leprae cosmid B2548	Mycobacterium leprae	38,177	27-Aug-99
		GB_PL1:EGGTPCHI	242	Z49757	E. gracilis mRNA for GTP cyclohydrolase I (core region).	Euglena gracilis	64,876	20-OCT-1995
αa01515	975	GB_BA1:ECOUW93	338534	U14003	Escherichia coli K-12 chromosomal region from 92.8 to 00.1 minutes.	Escherichia coli	38,943	17-Apr-96
		GB_BA1:ECOUW93	338534	U14003	Escherichia coli K-12 chromosomal region from 92.8 to 00.1 minutes.	Escherichia coli	37,500	17-Apr-96
		GB_BA1:MTCY49	39430	Z73966	Mycobacterium tuberculosis H37Rv complete genome; segment 93/162.	Mycobacterium tuberculosis	38,010	24-Jun-99
αa01516	513	GB_IN1:DMEZ38847	5419	AJ238847	Drosophila melanogaster mRNA for drosophila dodeca-satellite protein 1 (DDP-1).	Drosophila melanogaster	36,346	13-Aug-99
		GB_HTG3:AC009210	103814	AC009210	Drosophila melanogaster chromosome 2 clone BACR01106 (D1054) RPCI-98 01.1.6 map 55D-55D strain y; cn bw sp. *** SEQUENCING IN PROGRESS	Drosophila melanogaster	37,897	20-Aug-99
					***, 86 unordered pieces.			
αa01517	600	GB_IN2:AF132179	4842	AF132179	Drosophila melanogaster clone LD21677 unknown mRNA.	Drosophila melanogaster	36,149	3-Jun-99
		GB_PL2:F6H8	82596	AF178045	Arabidopsis thaliana BAC F6H8.	Arabidopsis thaliana	35,846	19-Aug-99
		GB_PL2:AF038831	647	AF038831	Sorosporium saponariae internal transcribed spacer 1, 5.8S ribosomal RNA gene; and internal transcribed spacer 2, complete sequence.	Sorosporium saponariae	40,566	13-Apr-99
		GB_PL2:ATAC005957	108355	AC005957	Arabidopsis thaliana chromosome II BAC T15J14 genomic sequence, complete sequence.	Arabidopsis thaliana	38,095	7-Jan-99
αa01521	921	GB_BA1:ANANIFBH	5936	J05111	Anabaena sp. (clone AnH20.1) nitrogen fixation operon nifB, fdxN, nifS, nifU, and nifH genes, complete cds.	Anabaena sp.	38,206	26-Apr-93
		GB_PR2:AC002461	197273	AC002461	Human BAC clone RG204116 from Tq31, complete sequence.	Homo sapiens	36,623	20-Aug-97
		GB_PR2:AC002461	197273	AC002461	Human BAC clone RG204116 from Tq31, complete sequence.	Homo sapiens	34,719	20-Aug-97
αa01528	651	GB_RO:MM437P9	165901	AL019866	Mus musculus chromosome X, clone 437P9.	Mus musculus	37,500	29-Jun-99
		GB_PR3:AC005740	186780	AC005740	Homo sapiens chromosome 5p, BAC clone 50g21 (LBNL H154), complete sequence.	Homo sapiens	37,031	01-OCT-1998
		GB_PR3:AC005740	186780	AC005740	Homo sapiens chromosome 5p, BAC clone 50g21 (LBNL H154), complete sequence.	Homo sapiens	38,035	01-OCT-1998
αa01551	1998	GB_BA1:MTCY22G10	35420	Z84724	Mycobacterium tuberculosis H37Rv complete genome; segment 21/162.	Mycobacterium tuberculosis	38,371	17-Jun-98
		GB_BA2:ECOUW89	176195	U00006	E. coli chromosomal region from 89.2 to 92.8 minutes.	Escherichia coli	38,064	17-DEC-1993
αa01561	1053	GB_BA1:SCQ11	15441	AL096823	Streptomyces coelicolor cosmid Q11	Streptomyces coelicolor	60,775	8-Jul-99
		GB_IN1:CEY62H9A	47396	AL032630	Caenorhabditis elegans cosmid Y62H9A, complete sequence.	Caenorhabditis elegans	38,514	2-Sep-99
		GB_PR4:HSU51003	3202	U51003	Homo sapiens DLX-2 (DLX-2) gene, complete cds.	Homo sapiens	37,730	07-DEC-1999
αa01599	1785	GB_OM:PIGDAO1	395	M18444	Pig D-amino acid oxidase (DAO) gene, exon 1.	Sus scrofa	39,340	27-Apr-93
		GB_BA1:MTCH125	37432	Z98268	Mycobacterium tuberculosis H37Rv complete genome; segment 76/162.	Mycobacterium tuberculosis	63,300	17-Jun-98
		GB_BA1:U00021	39193	U00021	Mycobacterium leprae cosmid L247.	Mycobacterium leprae	36,756	29-Sep-94

Table 4 (continued)

rx01617	795	GB_BA1:MLCB1351 GB_PR2:HSMTM0	38936 217657	Z95117 AL034384	Mycobacterium leprae cosmid B1351. Human chromosome Xq28, cosmid clones 7H3, 14D7, C1230, 11E7, F1096, A12197, 12G8, A09100; complete sequence bases 1..217657.	Mycobacterium leprae Homo sapiens	36,756 40,811	24-Jun-97 5-Jul-99
		GB_PR2:HS13D10	153147	AL021407	Homo sapiens DNA sequence from PAC 13D10 on chromosome 6p22.3-23. Contains CpG island.	Homo sapiens	38,768	23-Nov-99
		GB_PR2:HSMTM0	217657	AL034384	Human chromosome Xq28, cosmid clones 7H3, 14D7, C1230, 11E7, F1096, A12197, 12G8, A09100; complete sequence bases 1..217657.	Homo sapiens	39,018	5-Jul-99
rx01657	723	GB_BA1:MTCY1A10	25949	Z95387	Mycobacterium tuberculosis H37Rv complete genome; segment 117/162.	Mycobacterium tuberculosis	40,656	17-Jun-98
		GB_EST6:D79278	392	D79278	HUM213D06B Human aorta polyA+ (TFujiwara) Homo sapiens cDNA clone GEN-213D06 5', mRNA sequence.	Homo sapiens	44,262	9-Feb-96
		GB_BA2:AF129925	10243	AF129925	Thiobacillus ferrooxidans carboxysome operon, complete cds.	Thiobacillus ferrooxidans	40,709	17-MAY-1999
rx01660	675	GB_BA1:MTV013	11364	AL021309	Mycobacterium tuberculosis H37Rv complete genome; segment 134/162.	Mycobacterium tuberculosis	40,986	17-Jun-98
		GB_RO:MMFV1	6480	X97719	M. musculus retrovirus restriction gene Fv1.	Mus musculus	35,364	29-Aug-96
		GB_PAT:A67508	6480	A67508	Sequence 1 from Patent WO9743410.	Mus musculus	35,364	05-MAY-1999
rx01678	651	GB_VI:TVU95309	600	U95309	Tula virus O64 nucleocapsid protein gene, partial cds.	Tula virus	41,894	28-OCT-1997
		GB_VI:TVU95303	600	U95303	Tula virus O52 nucleocapsid protein gene, partial cds.	Tula virus	41,712	28-OCT-1997
		GB_VI:TVU95302	600	U95302	Tula virus O24 nucleocapsid protein gene, partial cds.	Tula virus	39,576	28-OCT-1997
rx01679	1359	GB_EST5:H91843	362	H91843	ys8te01.s1 Soares retina N2b4HR Homo sapiens cDNA clone IMAGE:221208 3' similar to gb:X63749_rna1 GUANINE NUCLEOTIDE-BINDING PROTEIN G(T), ALPHA-1 (HUMAN);, mRNA sequence.	Homo sapiens	39,157	29-Nov-95
		GB_STS:G26925	362	G26925	human STS SHGC-30023, sequence tagged site.	Homo sapiens	39,157	14-Jun-96
		GB_PL2:AF139451	1202	AF139451	Gossypium robinsonii CeaA2 pseudogene, partial sequence.	Gossypium robinsonii	38,910	1-Jun-99
rx01690	1224	GB_BA1:SC1C2	42210	AL031124	Streptomyces coelicolor cosmid 1C2.	Streptomyces coelicolor	60,644	15-Jan-99
		GB_EST22:A1064232	493	A1064232	GH04563.5prime GH Drosophila melanogaster head pOT2 Drosophila melanogaster cDNA clone GH04563 5prime, mRNA sequence.	Drosophila melanogaster	38,037	24-Nov-98
		GB_IN2:AF117896	1020	AF117896	Drosophila melanogaster neuropeptide F (npf) gene, complete cds.	Drosophila melanogaster	36,122	2-Jul-99
rx01692	873	GB_BA2:AF067123	1034	AF067123	Lactobacillus reuteri cobalamin biosynthesis protein J (cbiJ) gene, partial cds; and uroporphyrin-III C-methyltransferase (sumT) gene, complete cds.	Lactobacillus reuteri	48,079	3-Jun-98
		GB_RO:RATNFHPEP	3085	M37227	Rat heavy neurofilament (NF-H) polypeptide, partial cds.	Rattus norvegicus	37,093	27-Apr-93
		GB_RO:RSNFH	3085	X13804	Rat mRNA for heavy neurofilament polypeptide NF-H C-terminus.	Rattus sp.	37,093	14-Jul-95
rx01698	1353	GB_BA2:AF124600	4115	AF124600	Corynebacterium glutamicum chorismate synthase (aroC), shikimate kinase (aroK), and 3-dehydroquinate synthase (aroB) genes, complete cds; and putative cytoplasmic peptidase (pepQ) gene, partial cds.	Corynebacterium glutamicum	100,000	04-MAY-1999
		GB_BA1:MTCY159	33818	Z83863	Mycobacterium tuberculosis H37Rv complete genome; segment 111/162.	Mycobacterium tuberculosis	36,323	17-Jun-98

							Mycobacterium leprae cosmid B937 DNA sequence.				
693	rx01699	38914	L78820	GB_BA1:MSGB937C	4115	AF124600	Corynebacterium glutamicum chorismate synthase (aroC), shikimate kinase (aroK), and 3-dehydroquinate synthase (aroB) genes, complete cds; and putative cytoplasmic peptidase (pepQ) gene, partial cds.	Corynebacterium glutamicum	100,000	04-MAY-1999	
		41097	AF016585	GB_BA2:AF016585	41097	AF016585	Streptomyces caelestis cytochrome P-450 hydroxylase homolog (nidi) gene, partial cds; polyketide synthase modules 1 through 7 (nidA) genes, complete cds; and N-methyltransferase homolog gene, partial cds.	Streptomyces caelestis	40,260	07-DEC-1997	
		399	C19712	GB_EST9:C19712	399	C19712	C19712 Rice panicle at ripening stage Oryza sativa cDNA clone E10821_1A, mRNA sequence.	Oryza sativa	45,425	24-OCT-1996	
805	rx01712	278	AA952466	GB_EST21:AA952466	278	AA952466	TENS1404 T. cruzi epimastigote normalized cDNA Library Trypanosoma cruzi cDNA clone 1404 5', mRNA sequence.	Trypanosoma cruzi	40,876	29-OCT-1998	
		278	AA952466	GB_EST21:AA952466	278	AA952466	TENS1404 T. cruzi epimastigote normalized cDNA Library Trypanosoma cruzi cDNA clone 1404 5', mRNA sequence.	Trypanosoma cruzi	41,367	29-OCT-1998	
684	rx01719	154416	AL109925	GB_HTG1:HSDJ534K	154416	AL109925	Homo sapiens chromosome 1 clone RP4-534K7, *** SEQUENCING IN PROGRESS ***, in unordered pieces.	Homo sapiens	35,651	23-Nov-99	
		154416	AL109925	GB_HTG1:HSDJ534K	154416	AL109925	Homo sapiens chromosome 1 clone RP4-534K7, *** SEQUENCING IN PROGRESS ***, in unordered pieces.	Homo sapiens	35,651	23-Nov-99	
1332	rx01720	431	A1447108	GB_EST27:A1447108	431	A1447108	m91e08.x1 Stratagene mouse heart (#937316) Mus musculus cDNA clone IMAGE:566118 3', mRNA sequence.	Mus musculus	39,671	09-MAR-1999	
		179640	AC006322	GB_PR4:AC006322	179640	AC006322	Homo sapiens PAC clone DJ1060B11 from 7q11.23-q21.1, complete sequence.	Homo sapiens	35,817	18-MAR-1999	
		106184	AF013294	GB_PL2:TM018A10	106184	AF013294	Arabidopsis thaliana BAC TM018A10.	Arabidopsis thaliana	35,698	12-Jul-97	
		179640	AC006322	GB_PR4:AC006322	179640	AC006322	Homo sapiens PAC clone DJ1060B11 from 7q11.23-q21.1, complete sequence.	Homo sapiens	37,243	18-MAR-1999	
876	rx01746	443	R46227	GB_EST3:R46227	443	R46227	y952a03.s1 Soares infant brain 1NIB Homo sapiens cDNA clone IMAGE:36000 3', mRNA sequence.	Homo sapiens	42,812	22-MAY-1995	
		443	R46227	GB_EST3:R46227	443	R46227	y952a03.s1 Soares infant brain 1NIB Homo sapiens cDNA clone IMAGE:36000 3', mRNA sequence.	Homo sapiens	42,655	22-MAY-1995	
1167	rx01747	34150	Z70283	GB_BA1:MTCY190	34150	Z70283	Mycobacterium tuberculosis H37Rv complete genome, segment 98/162.	Mycobacterium tuberculosis	59,294	17-Jun-98	
		40281	Z98741	GB_BA1:MLCB22	40281	Z98741	Mycobacterium leprae cosmid B22.	Mycobacterium leprae	57,584	22-Aug-97	
		40024	AL096872	GB_BA1:SC5F7	40024	AL096872	Streptomyces coelicolor cosmid 5F7.	Streptomyces coelicolor A3(2)	61,810	22-Jul-99	
924	rx01757	416	AA918454	GB_EST21:AA918454	416	AA918454	om38c02.s1 Soares_NFL_T_GBC_S1 Homo sapiens cDNA clone IMAGE:1543298 3' similar to WP.F28F8.3 CE09757 SMALL NUCLEAR RIBONUCLEOPROTEIN E., mRNA sequence.	Homo sapiens	39,655	23-Jun-98	
		345	H34042	GB_EST4:H34042	345	H34042	EST110563 Rat PC-12 cells, NGF-treated (9 days) Rattus sp. cDNA clone RPNB181 5' end, mRNA sequence.	Rattus sp.	35,942	2-Apr-98	
		450	AA899038	GB_EST20:AA899038	450	AA899038	NCP6G8T7 Perithelial Neurospora crassa cDNA clone NP6G8 3' end, mRNA sequence.	Neurospora crassa	40,000	12-Apr-98	

Table 4 (continued)

αa01807	915	GB_BA1:AP000063 GB_HTG4:AC010694	185300 115857	AP000063 AC010694	Aeropyrum pernix genomic DNA, section 67. Drosophila melanogaster clone RPC198-6H2, *** SEQUENCING IN PROGRESS ***, 75 unordered pieces.	Aeropyrum pernix Drosophila melanogaster	40,067 35,450	22-Jun-99 16-OCT-1999
αa01821	401	GB_HTG4:AC010694 GB_BA1:CGL007732	115857 4460	AC010694 AJ007732	Drosophila melanogaster clone RPC198-6H2, *** SEQUENCING IN PROGRESS ***, 75 unordered pieces. Corynebacterium glutamicum 3' ppc gene, secG gene, amt gene, ocd gene and 5' soxA gene.	Drosophila melanogaster Corynebacterium glutamicum	35,450 100,000	16-OCT-1999 7-Jan-99
αa01835	654	GB_RO:RATALGL GB_OV:APIGY2 GB_EST30:AI629479	7601 1381 353	M24108 X78272 AI629479	Rattus norvegicus (clone A2U42) alpha2u globulin gene, exons 1-7. Anas platyrhynchos (Super M) IgY upslon heavy chain gene, exon 2. 486101D10 x1 486 - leaf primordia cDNA library from Hake lab Zea mays cDNA, mRNA sequence.	Rattus norvegicus Anas platyrhynchos Zea mays	38,692 36,962 38,109	15-DEC-1994 15-Feb-99 26-Apr-99
αa01850	1470	GB_ST5:G48245 GB_GSS3:B49052 GB_BA2:ECOUW67_0	515 515 110000	G48245 B49052 U18997	SHGC-62915 Human Homo sapiens STS genomic, sequence tagged site. RPC111-4112 TV RPC1-11 Homo sapiens genomic clone RPC1-11-4112, genomic survey sequence. Escherichia coli K-12 chromosomal region from 67.4 to 76.0 minutes.	Homo sapiens Homo sapiens Escherichia coli	37,021 37,021 37,196	26-MAR-1999 8-Apr-99 U18997
αa01878	1002	GB_HTG1:CEY64F11 GB_HTG1:CEY64F11 GB_HTG1:CEY64F11	177748 177748 177748	Z99776 Z99776 Z99776	Caenorhabditis elegans chromosome IV clone Y64F11, *** SEQUENCING IN PROGRESS ***, in unordered pieces. Caenorhabditis elegans chromosome IV clone Y64F11, *** SEQUENCING IN PROGRESS ***, in unordered pieces. Caenorhabditis elegans chromosome IV clone Y64F11, *** SEQUENCING IN PROGRESS ***, in unordered pieces.	Caenorhabditis elegans Caenorhabditis elegans Caenorhabditis elegans	37,564 37,564 37,576	14-OCT-1998 14-OCT-1998 14-OCT-1998
αa01892	852	GB_BA1:MTCY274 GB_BA1:MLCB250 GB_BA1:MSG81529C	39991 40603 36985	Z74024 Z97369 L78824	Mycobacterium tuberculosis H37Rv complete genome, segment 126/162. Mycobacterium leprae cosmid B250. Mycobacterium leprae cosmid B1529 DNA sequence.	Mycobacterium tuberculosis Mycobacterium leprae Mycobacterium leprae	35,910 64,260 64,260	19-Jun-98 27-Aug-99 15-Jun-96
αa01894	978	GB_BA1:MTCY274 GB_IN1:CELLF46H5 GB_HTG3:AC009204	39991 38886 115633	Z74024 U41543 AC009204	Mycobacterium tuberculosis H37Rv complete genome, segment 126/162. Caenorhabditis elegans cosmid F46H5. Drosophila melanogaster chromosome 2 clone BACR03E19 (D1033) RPC1-98 03.E.19 map 36E-37C strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***, 94 unordered pieces.	Mycobacterium tuberculosis Caenorhabditis elegans Drosophila melanogaster	37,229 38,525 31,579	19-Jun-98 29-Nov-96 18-Aug-99
αa01920	1125	GB_BA2:AF112536 GB_BA1:CANRDFGE	1798 6054	AF112536 Y09572	Corynebacterium glutamicum ribonucleotide reductase beta-chain (nrdF) gene, complete cds. Corynebacterium ammoniagenes nrdH, nrdI, nrdE, nrdF genes.	Corynebacterium glutamicum Corynebacterium ammoniagenes	99,733 70,321	5-Aug-99 18-Apr-98

BNSDOCID: <WO 0100843A2 I_>

Table 4 (continued)

ra02085	2358	GB_BA1:MTCY22G8	22550	Z95585	Mycobacterium tuberculosis H37Rv complete genome; segment 49/162.	Mycobacterium tuberculosis	38,442	17-Jun-98
		GB_BA1:MLCB33	42224	Z94723	Mycobacterium leprae cosmid B33.	Mycobacterium leprae	56,486	24-Jun-97
		GB_BA1:ECOUW85	91414	M87049	E. coli genomic sequence of the region from 84.5 to 86.5 minutes.	Escherichia coli	52,127	29-MAY-1995
ra02093	927	GB_EST14:AA448146	452	AA448146	zw82h01.r1 Soares_testis_NHT Homo sapiens cDNA clone IMAGE:782737	Homo sapiens	34,163	4-Jun-97
		GB_EST17:AA641937	444	AA641937	5', mRNA sequence.	Homo sapiens	35,586	27-OCT-1997
		GB_PR3:AC003074	143029	AC003074	5', mRNA sequence.	Homo sapiens	31,917	6-Nov-97
ra02106	1179	GB_BA1:SC1A6	37620	AL023496	Human PAC clone DJ0596009 from 7p15, complete sequence.	Streptomyces coelicolor	35,818	13-Jan-99
		GB_PR4:AC005553	179651	AC005553	Streptomyces coelicolor cosmid 1A6.	Homo sapiens	34,274	31-DEC-1998
		GB_EST3:R49746	397	R49746	Homo sapiens chromosome 17, clone hRPK.112_J_9, complete sequence.	Homo sapiens	41,162	18-MAY-1995
		GB_BA1:SC6G10	36734	AL049497	y971g10.r1 Soares infant brain 1N1B Homo sapiens cDNA clone IMAGE:38768 5' similar to gb:V00567 BETA-2-MICROGLOBULIN PRECURSOR (HUMAN); mRNA sequence.	Streptomyces coelicolor	50,791	24-MAR-1999
ra02111	1407	GB_BA1:U00010	41171	U00010	Streptomyces coelicolor cosmid 6G10.	Mycobacterium leprae	37,563	01-MAR-1994
		GB_BA1:MTCY336	32437	Z95586	Mycobacterium leprae cosmid B1170.	Mycobacterium tuberculosis	39,504	24-Jun-99
ra02112	960	GB_HTG3:AC010579	157658	AC010579	Mycobacterium tuberculosis H37Rv complete genome; segment 70/162.	Drosophila melanogaster	37,909	24-Sep-99
		GB_GSS3:B09839	1191	B09839	Drosophila melanogaster chromosome 3 clone BACR09D08 (D1101) RPCI-98 Drosophila melanogaster 09.D.8 map 96F-96F strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***; 121 unordered pieces.	Arabidopsis thaliana	37,843	14-MAY-1997
		GB_HTG3:AC010579	157658	AC010579	T12A12-Sp6 TAMU Arabidopsis thaliana genomic clone T12A12, genomic survey sequence.	Drosophila melanogaster	37,909	24-Sep-99
ra02134	1044	GB_BA1:SCSECYDN	6154	X83011	09.D.8 map 96F-96F strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***; 121 unordered pieces.	Streptomyces coelicolor	36,533	02-MAR-1998
		GB_EST32:A1731596	568	A1731596	S.coelicolor secY locus DNA.	Gossypium hirsutum	33,451	11-Jun-99
		GB_BA1:SCSECYDN	6154	X83011	BNLGH10185 Six-day Cotton fiber Gossypium hirsutum cDNA 5' similar to (AC004005) putative ribosomal protein L7 [Arabidopsis thaliana], mRNA sequence.	Streptomyces coelicolor	36,756	02-MAR-1998
ra02135	1197	GB_PR3:HS525L6	168111	AL023807	S.coelicolor secY locus DNA.	Homo sapiens	34,365	23-Nov-99
		GB_PL2:ATF21P8	85785	AL022347	Human DNA sequence from clone RP3-525L6 on chromosome 6p22.3-23 Contains CA repeat, STSs, GSSs and a CpG island, complete sequence.	Arabidopsis thaliana	34,325	9-Jun-99
		GB_PL2:U89959	106973	U89959	Arabidopsis thaliana DNA chromosome 4, BAC clone F21P8 (ESSA project).	Arabidopsis thaliana	33,874	26-Jun-98

Table 4 (continued)

αa02136	645	GB_PL2:ATAC005819	57752	AC005819	Arabidopsis thaliana chromosome II BAC T3A4 genomic sequence, complete sequence.	Arabidopsis thaliana	34,123	3-Nov-98
		GB_PL2:F15K9	71097	AC005278	Arabidopsis thaliana chromosome 1 BAC F15K9 sequence, complete sequence.	Arabidopsis thaliana	31,260	7-Nov-98
αa02139	1962	GB_PL2:U89959	106973	U89959	Arabidopsis thaliana BAC T7123, complete sequence.	Arabidopsis thaliana	34,281	26-Jun-98
		GB_BA1:MTCY190	34150	Z70283	Mycobacterium tuberculosis H37Rv complete genome, segment 98/162.	Mycobacterium tuberculosis	62,904	17-Jun-98
		GB_BA1:MSG81554C	36548	L78814	Mycobacterium leprae cosmid B1554 DNA sequence.	Mycobacterium leprae	36,648	15-Jun-96
		GB_BA1:MSG81551C	36548	L78813	Mycobacterium leprae cosmid B1551 DNA sequence.	Mycobacterium leprae	36,648	15-Jun-96
αa02153	903	GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	99,104	1-Jul-98
		GB_BA1:AF005242	1044	AF005242	Corynebacterium glutamicum N-acetylglutamate-5-semialdehyde dehydrogenase (argC) gene, complete cds.	Corynebacterium glutamicum	99,224	2-Jul-97
		GB_BA1:CGARGCJB	4355	X86157	C glutamicum argC, argJ, argB, argD, and argF genes.	Corynebacterium glutamicum	100,000	25-Jul-96
αa02154	414	GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	98,551	1-Jul-98
		GB_BA1:AF005242	1044	AF005242	Corynebacterium glutamicum N-acetylglutamate-5-semialdehyde dehydrogenase (argC) gene, complete cds.	Corynebacterium glutamicum	98,477	2-Jul-97
		GB_BA1:CGARGCJB	4355	X86157	C glutamicum argC, argJ, argB, argD, and argF genes.	Corynebacterium glutamicum	100,000	25-Jul-96
αa02155	1287	GB_BA1:CGARGCJB	4355	X86157	C glutamicum argC, argJ, argB, argD, and argF genes.	Corynebacterium glutamicum	99,767	25-Jul-96
		GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	99,378	1-Jul-98
		GB_BA1:MSG81133C	42106	L78811	Mycobacterium leprae cosmid B1133 DNA sequence.	Mycobacterium leprae	55,504	15-Jun-96
αa02156	1074	GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	100,000	1-Jul-98

Table 4 (continued)

rx02157	1296	GB_BA1:CGARGCJB D	4355	X86157	C glutamicum argC, argJ, argB, argD, and argF genes.	Corynebacterium glutamicum	100,000	25-Jul-96
		GB_BA2:AE001816	10007	AE001816	Thermotoga maritima section 128 of 136 of the complete genome.	Thermotoga maritima	50,238	2-Jun-99
		GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	99,612	1-Jul-98
		GB_BA1:CGARGCJB D	4355	X86157	C glutamicum argC, argJ, argB, argD, and argF genes.	Corynebacterium glutamicum	99,612	25-Jul-96
		GB_BA1:MTCY06H11	38000	Z85982	Mycobacterium tuberculosis H37Rv complete genome; segment 73/162.	Mycobacterium tuberculosis	57,278	17-Jun-98
rx02158	1080	GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	100,000	1-Jul-98
		GB_BA2:AF031518	2045	AF031518	Corynebacterium glutamicum ornithine carbamoyltransferase (argF) gene, complete cds.	Corynebacterium glutamicum	99,898	5-Jan-99
rx02159	636	GB_BA1:CGARGCJB D	4355	X86157	C glutamicum argC, argJ, argB, argD, and argF genes.	Corynebacterium glutamicum	100,000	25-Jul-96
		GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	99,843	1-Jul-98
		GB_BA2:AF031518	2045	AF031518	Corynebacterium glutamicum ornithine carbamoyltransferase (argF) gene, complete cds.	Corynebacterium glutamicum	88,679	5-Jan-99
		GB_BA2:AF041436	516	AF041436	Corynebacterium glutamicum arginine repressor (argR) gene, complete cds.	Corynebacterium glutamicum	100,000	5-Jan-99
rx02160	1326	GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	99,774	1-Jul-98
		GB_BA2:AF030520	1206	AF030520	Corynebacterium glutamicum argininosuccinate synthetase (argG) gene, complete cds.	Corynebacterium glutamicum	99,834	19-Nov-97
rx02162	1554	GB_BA1:SCARGGH	1909	Z49111	S. clavuligerus argG gene and argH gene (partial).	Streptomyces clavuligerus	65,913	22-Apr-96
		GB_BA2:AF049897	9196	AF049897	Corynebacterium glutamicum N-acetylglutamylphosphate reductase (argC), ornithine acetyltransferase (argJ), N-acetylglutamate kinase (argB), acetylornithine transaminase (argD), ornithine carbamoyltransferase (argF), arginine repressor (argR), argininosuccinate synthase (argG), and argininosuccinate lyase (argH) genes, complete cds.	Corynebacterium glutamicum	88,524	1-Jul-98

Table 4 (continued)

GB_BA2:AF048764	1437	AF048764	Corynebacterium glutamicum argininosuccinate lyase (argH) gene, complete cds.	Corynebacterium glutamicum	87,561	1-Jul-98
GB_BA1:MTCY06H11	38000	Z85982	Mycobacterium tuberculosis H37Rv complete genome; segment 73/162.	Mycobacterium tuberculosis	64,732	17-Jun-98
GB_BA1:MTCY31	37630	Z73101	Mycobacterium tuberculosis H37Rv complete genome; segment 41/162.	Mycobacterium tuberculosis	36,998	17-Jun-98
GB_BA1:CGGLTG	3013	X66112	C. glutamicum glt gene for citrate synthase and ORF.	Corynebacterium glutamicum	39,910	17-Feb-95
GB_PL2:PGU65399	2700	U65399	Basidiomycete CECT 20197 phenoloxidase (pox1) gene, complete cds.	basidiomycete CECT 20197	38,474	19-Jul-97
GB_PR3:AC002468	115888	AC002468	Human Chromosome 15q26.1 PAC clone pDJ417d7, complete sequence.	Homo sapiens	35,941	16-Sep-98
GB_BA1:MSG81970C	39399	L78815	Mycobacterium leprae cosmid B1970 DNA sequence.	Mycobacterium leprae	40,286	15-Jun-96
GB_PR3:AC002468	115888	AC002468	Human Chromosome 15q26.1 PAC clone pDJ417d7, complete sequence.	Homo sapiens	33,689	16-Sep-98
GB_BA1:BRLASPA	1987	D25316	Brevibacterium flavum aspA gene for aspartase, complete cds.	Corynebacterium glutamicum	99,353	6-Feb-99
GB_PAT:E04307	1581	E04307	DNA encoding Brevibacterium flavum aspartase.	Corynebacterium glutamicum	99,367	29-Sep-97
GB_BA1:ECOUW93	338534	U14003	Escherichia coli K-12 chromosomal region from 92.8 to 00.1 minutes.	Escherichia coli	37,651	17-Apr-96
GB_BA2:AF050166	840	AF050166	Corynebacterium glutamicum ATP phosphoribosyltransferase (hisG) gene, complete cds.	Corynebacterium glutamicum	98,214	5-Jan-99
GB_BA1:BRLASPA	1987	D25316	Brevibacterium flavum aspA gene for aspartase, complete cds.	Corynebacterium glutamicum	93,805	6-Feb-99
GB_PAT:E08649	188	E08649	DNA encoding part of aspartase from coryneform bacteria.	Corynebacterium glutamicum	100,000	29-Sep-97
GB_BA2:AF086704	264	AF086704	Corynebacterium glutamicum phosphoribosyl-ATP-pyrophosphohydrolase (hisE) gene, complete cds.	Corynebacterium glutamicum	100,000	8-Feb-99
GB_BA1:EAY17145	6019	Y17145	Eubacterium acidaminophilum grdR, grdI, grdH genes and partial ldc, grdT genes.	Eubacterium acidaminophilum	39,075	5-Aug-98
GB_STS:G01195	332	G01195	fruit fly STS Dm1930 clone DS06959 T7.	Drosophila melanogaster	35,542	28-Feb-95
GB_BA1:MTCY261	27322	Z97559	Mycobacterium tuberculosis H37Rv complete genome; segment 95/162.	Mycobacterium tuberculosis	33,938	17-Jun-98
GB_BA1:MLCB2533	40245	AL035310	Mycobacterium leprae cosmid B2533.	Mycobacterium leprae	65,517	27-Aug-99
GB_BA1:U00017	42157	U00017	Mycobacterium leprae cosmid B2126.	Mycobacterium leprae	36,770	01-MAR-1994
GB_BA1:U00017	42157	U00017	Mycobacterium leprae cosmid B2126.	Mycobacterium leprae	38,674	01-MAR-1994
GB_BA1:MLCB2533	40245	AL035310	Mycobacterium leprae cosmid B2533.	Mycobacterium leprae	65,465	27-Aug-99
GB_BA1:MTCY261	27322	Z97559	Mycobacterium tuberculosis H37Rv complete genome; segment 95/162.	Mycobacterium tuberculosis	37,577	17-Jun-98
GB_BA1:U00017	42157	U00017	Mycobacterium leprae cosmid B2126.	Mycobacterium leprae	59,823	01-MAR-1994
GB_BA1:AP000063	185300	AP000063	Aeropyrum pernix genomic DNA, section 6/7.	Aeropyrum pernix	39,442	22-Jun-99

Table 4 (continued)

rx022229	948	GB_PR4:AC006236	127593	AC006236	Homo sapiens chromosome 17, clone hCIT.162_E_12, complete sequence.	Homo sapiens	37,191	29-DEC-1998
		GB_BA1:MSGY154	40221	AD000002	Mycobacterium tuberculosis sequence from clone y154.	Mycobacterium tuberculosis	53,541	03-DEC-1996
		GB_BA1:MTCY154	13935	Z98209	Mycobacterium tuberculosis H37Rv complete genome, segment 121/162.	Mycobacterium tuberculosis	40,407	17-Jun-98
rx022234	3462	GB_BA1:U00019	36033	U00019	Mycobacterium leprae cosmid B2235.	Mycobacterium leprae	40,541	01-MAR-1994
		GB_BA1:MSGB937C	38914	L78820	Mycobacterium leprae cosmid B937 DNA sequence	Mycobacterium leprae	66,027	15-Jun-96
		GB_BA1:MTCY2B12	20431	Z81011	Mycobacterium tuberculosis H37Rv complete genome, segment 61/162.	Mycobacterium tuberculosis	71,723	18-Jun-98
		GB_BA2:U01072	4393	U01072	Mycobacterium bovis BCG oritidine-5'-monophosphate decarboxylase (uraA) gene.	Mycobacterium bovis	67,101	22-DEC-1993
rx022235	727	GB_BA1:MSU91572	960	U91572	Mycobacterium smegmatis carbamoyl phosphate synthetase (pyrAB) gene, partial cds and oritidine 5'-monophosphate decarboxylase (pyrF) gene, complete cds.	Mycobacterium smegmatis	60,870	22-MAR-1997
		GB_HTG3:AC009364	192791	AC009364	Homo sapiens chromosome 7, *** SEQUENCING IN PROGRESS ***	Homo sapiens	37,994	1-Sep-99
		GB_HTG3:AC009364	192791	AC009364	Homo sapiens chromosome 7, *** SEQUENCING IN PROGRESS ***	Homo sapiens	37,994	1-Sep-99
rx022237	693	GB_BA1:MTCY21B4	39150	Z80108	Mycobacterium tuberculosis H37Rv complete genome, segment 62/162.	Mycobacterium tuberculosis	55,844	23-Jun-98
		GB_BA2:AF077324	5228	AF077324	Rhodococcus equi strain 103 plasmid RE-VP1 fragment f.	Rhodococcus equi	41,185	5-Nov-98
		GB_EST22:AU017763	586	AU017763	AU017763 Mouse two-cell stage embryo cDNA Mus musculus cDNA clone J0744A04 3', mRNA sequence.	Mus musculus	38,616	19-OCT-1998
rx022239	1389	GB_BA1:MTCY21B4	39150	Z80108	Mycobacterium tuberculosis H37Rv complete genome, segment 62/162.	Mycobacterium tuberculosis	56,282	23-Jun-98
		GB_HTG3:AC010745	193862	AC010745	Homo sapiens clone NH0549D18, *** SEQUENCING IN PROGRESS ***	Homo sapiens	36,772	21-Sep-99
		GB_HTG3:AC010745	193862	AC010745	Homo sapiens clone NH0549D18, *** SEQUENCING IN PROGRESS ***	Homo sapiens	36,772	21-Sep-99
rx022240	1344	EM_PAT:E09855	1239	E09855	gDNA encoding S-adenosylmethionine synthetase.	Corynebacterium glutamicum	99,515	07-OCT-1997 (Rel. 52, Created)
		GB_PAT:A37831	5392	A37831	Sequence 1 from Patent WO9408014.	Streptomyces pristinaespiralis	63,568	05-MAR-1997
		GB_BA2:AF117274	2303	AF117274	Streptomyces spectabilis flavoprotein homolog Dfp (dfp) gene, partial cds; and Streptomyces spectabilis S-adenosylmethionine synthetase (meiK) gene, complete cds.	Streptomyces spectabilis	65,000	31-MAR-1999
rx022246	1107	EM_BA1:AB003693	5589	AB003693	Corynebacterium ammoniagenes DNA for rib operon, complete cds.	Corynebacterium ammoniagenes	52,909	03-OCT-1997 (Rel. 52, Created)

Table 4 (continued)

Table 4 (continued)

GB_EST23:AI128623	363	AI128623	qa62c01.s1 Soares_fetal_heart_NbH19W Homo sapiens cDNA clone IMAGE:1691328 3', mRNA sequence.	Homo sapiens	37,017	05-OCT-1998
GB_PL2:ATAC007019	102335	AC007019	Arabidopsis thaliana chromosome II BAC F7D8 genomic sequence, complete sequence.	Arabidopsis thaliana	33,988	16-MAR-1999
GB_BA2:AF116184	540	AF116184	Corynebacterium glutamicum L-aspartate-alpha-decarboxylase precursor (panD) gene, complete cds.	Corynebacterium glutamicum	100,000	02-MAY-1999
GB_GSS9:AQ164310	507	AQ164310	HS_2171_A2_E01_MR CIT Approved Human Genomic Sperm Library D Homo sapiens genomic clone Plate=2171 Col=2 Row=1, genomic survey sequence.	Homo sapiens	37,278	16-OCT-1998
GB_VI:MH68TKH	4557	X93468	Murine herpesvirus type 68 thymidine kinase and glycoprotein H genes.	murine herpesvirus 68	40,288	3-Sep-96
GB_HTG4:AC006091	176878	AC006091	Drosophila melanogaster chromosome 3 clone BACR48G05 (D475) RPCI-98 PROGRESS ***, 4 unordered pieces.	Drosophila melanogaster	36,454	27-OCT-1999
GB_HTG4:AC006091	176878	AC006091	Drosophila melanogaster chromosome 3 clone BACR48G05 (D475) RPCI-98 PROGRESS ***, 4 unordered pieces.	Drosophila melanogaster	36,454	27-OCT-1999
GB_BA2:RRU65510	16259	U65510	Rhodospirillum rubrum CO-induced hydrogenase operon (cooM, cooK, cooL, cooX, cooU, cooH) genes, iron sulfur protein (cooF) gene, carbon monoxide dehydrogenase (cooS) gene, carbon monoxide dehydrogenase accessory proteins (cooC, cooT, cooJ) genes, putative transcriptional activator (cooA) gene, nicotinate-nucleotide pyrophosphorylase (nadC) gene, complete cds, L-aspartate oxidase (nadB) gene, and alkyl hydroperoxide reductase (ahpC) gene, partial cds.	Rhodospirillum rubrum	37,828	9-Apr-97
GB_BA1:MSGY224	40051	AD000004	Mycobacterium tuberculosis sequence from clone y224.	Mycobacterium tuberculosis	49,418	03-DEC-1996
GB_BA1:MTY25D10	40838	Z95558	Mycobacterium tuberculosis H37Rv complete genome, segment 28/162.	Mycobacterium tuberculosis	49,360	17-Jun-98
GB_BA1:MSGY224	40051	AD000004	Mycobacterium tuberculosis sequence from clone y224.	Mycobacterium tuberculosis	38,150	03-DEC-1996
GB_HTG3:AC011348	111083	AC011348	Homo sapiens chromosome 5 clone CIT-HSPC_303E13, *** SEQUENCING IN PROGRESS ***, 3 ordered pieces.	Homo sapiens	35,821	06-OCT-1999
GB_HTG3:AC011348	111083	AC011348	Homo sapiens chromosome 5 clone CIT-HSPC_303E13, *** SEQUENCING IN PROGRESS ***, 3 ordered pieces.	Homo sapiens	35,821	06-OCT-1999
GB_HTG3:AC011412	89234	AC011412	Homo sapiens chromosome 5 clone CIT978SKB_81K21, *** SEQUENCING IN PROGRESS ***, 3 ordered pieces.	Homo sapiens	36,181	06-OCT-1999
GB_BA1:MSGY224	40051	AD000004	Mycobacterium tuberculosis sequence from clone y224.	Mycobacterium tuberculosis	37,792	03-DEC-1996
GB_BA1:MTY25D10	40838	Z95558	Mycobacterium tuberculosis H37Rv complete genome, segment 28/162.	Mycobacterium tuberculosis	37,792	17-Jun-98
GB_EST23:AI117213	476	AI117213	ub83h02.r1 Soares 2NbMT Mus musculus cDNA clone IMAGE:1395123 5', mRNA sequence.	Mus musculus	35,084	2-Sep-98

Table 4 (continued)

αa02345	1320	GB_BA1:BAPURKE	2582	X91189	B. ammoniagenes purK and purE genes.	Corynebacterium ammoniagenes	61,731	14-Jan-97
		GB_BA1:MTCY71	42729	Z92771	Mycobacterium tuberculosis H37Rv complete genome, segment 141/162.	Mycobacterium tuberculosis	39,624	10-Feb-99
		GB_BA1:MTCY71	42729	Z92771	Mycobacterium tuberculosis H37Rv complete genome, segment 141/162.	Mycobacterium tuberculosis	39,847	10-Feb-99
αa02350	618	GB_BA1:BAPURKE	2582	X91189	B. ammoniagenes purK and purE genes.	Corynebacterium ammoniagenes	64,286	14-Jan-97
		GB_PL1:SC130KBXV	129528	X94335	S. cerevisiae 130kb DNA fragment from chromosome XV.	Saccharomyces cerevisiae	36,617	15-Jul-97
		GB_PL1:SCXVORFS	50984	X90518	S. cerevisiae DNA of 51 Kb from chromosome XV right arm.	Saccharomyces cerevisiae	36,617	1-Nov-95
αa02373	1038	GB_PAT:E00311	1853	E00311	DNA coding of 2,5-diketogluconic acid reductase.	unidentified	56,123	29-Sep-97
		GB_PAT:I06030	1853	I06030	Sequence 4 from Patent EP 0305608.	Unknown.	56,220	02-DEC-1994
		GB_PAT:I00836	1853	I00836	Sequence 1 from Patent US 4758514.	Unknown.	56,220	21-MAY-1993
αa02375	1350	GB_BA2:CGU31230	3005	U31230	Corynebacterium glutamicum Obg protein homolog gene, partial cds, gamma glutamyl kinase (proB) gene, complete cds, and (unkdh) gene, complete cds.	Corynebacterium glutamicum	99,332	2-Aug-96
		GB_HTG3:AC009946	169072	AC009946	Homo sapiens clone NH0012C17, *** SEQUENCING IN PROGRESS ***; 1 unordered pieces.	Homo sapiens	36,115	8-Sep-99
		GB_HTG3:AC009946	169072	AC009946	Homo sapiens clone NH0012C17, *** SEQUENCING IN PROGRESS ***; 1 unordered pieces.	Homo sapiens	36,115	8-Sep-99
αa02380	777	GB_BA1:MTCY253	41230	Z81368	Mycobacterium tuberculosis H37Rv complete genome, segment 106/162.	Mycobacterium tuberculosis	38,088	17-Jun-98
		GB_HTG4:AC010658	120754	AC010658	Drosophila melanogaster chromosome 3L75C1 clone RPC198-3B20, *** SEQUENCING IN PROGRESS ***; 78 unordered pieces.	Drosophila melanogaster	35,817	16-OCT-1999
		GB_HTG4:AC010658	120754	AC010658	Drosophila melanogaster chromosome 3L75C1 clone RPC198-3B20, *** SEQUENCING IN PROGRESS ***; 78 unordered pieces.	Drosophila melanogaster	35,817	16-OCT-1999
αa02382	1419	GB_BA1:CGPROAGE	1783	X82929	C. glutamicum proA gene.	Corynebacterium glutamicum	98,802	23-Jan-97
		GB_BA1:MTCY428	26914	Z81451	Mycobacterium tuberculosis H37Rv complete genome, segment 107/162.	Mycobacterium tuberculosis	38,054	17-Jun-98
		GB_BA2:CGU31230	3005	U31230	Corynebacterium glutamicum Obg protein homolog gene, partial cds, gamma glutamyl kinase (proB) gene, complete cds, and (unkdh) gene, complete cds.	Corynebacterium glutamicum	98,529	2-Aug-96
αa02400	693	GB_BA1:CGACEA	2427	X75504	C. glutamicum aceA gene and thiX genes (partial).	Corynebacterium glutamicum	100,000	9-Sep-94
		GB_PAT:I86191	2135	I86191	Sequence 3 from patent US 5700661.	Unknown.	100,000	10-Jun-98
		GB_PAT:I13693	2135	I13693	Sequence 3 from patent US 5439822.	Unknown.	100,000	26-Sep-95
αa02432	1098	GB_GSS15:AQ60684	574	AQ606842	HS_5404_B2_E07_T7A RPC1-11 Human Male BAC Library Homo sapiens genomic clone Plate=980 Col=14 Row=J, genomic survey sequence.	Homo sapiens	39,716	10-Jun-99

Table 4 (continued)

1413	1413	GB_EST1:T05804	406	T05804	EST03693 Fetal brain, Stratagene (cat#936206) Homo sapiens cDNA clone HFBG63 similar to EST containing Alu repeat, mRNA sequence.	Homo sapiens	37,915	30-Jun-93
1554	1554	GB_PL1:AB006699	77363	AB006699	Arabidopsis thaliana genomic DNA, chromosome 5, p1 clone: MDJ22, complete sequence.	Arabidopsis thaliana	35,526	20-Nov-99
1554	1554	GB_BA2:AF114233	1852	AF114233	Corynebacterium glutamicum 5-enolpyruvylshikimate 3-phosphate synthase (aroA) gene, complete cds.	Corynebacterium glutamicum	100,000	7-Feb-99
1554	1554	GB_EST37:AW013061	578	AW013061	ODT-0033 Winter flounder ovary Pleuronectes americanus cDNA clone ODT-0033 5' similar to FRUCTOSE-BISPHOSPHATE ALDOLASE B (LIVER), mRNA sequence.	Pleuronectes americanus	39,175	10-Sep-99
1554	1554	GB_GSS15:AQ650027	728	AQ650027	Sheared DNA-5L2, TF Sheared DNA Trypanosoma brucei genomic clone Sheared DNA-5L2, genomic survey sequence.	Trypanosoma brucei	39,281	22-Jun-99
1554	1554	GB_BA1:MTCY359	36021	Z83859	Mycobacterium tuberculosis H37Rv complete genome, segment 84/162.	Mycobacterium tuberculosis	39,634	17-Jun-98
1554	1554	GB_BA1:MLCB1788	39228	AL008609	Mycobacterium leprae cosmid B1788.	Mycobacterium leprae	59,343	27-Aug-99
1554	1554	GB_BA1:SCAJ10601	4692	AJ010601	Streptomyces coelicolor A3(2) DNA for whiD and whiK loci.	Streptomyces coelicolor	48,899	17-Sep-98
1554	1554	GB_BA2:CGU31224	422	U31224	Corynebacterium glutamicum (ppx) gene, partial cds.	Corynebacterium glutamicum	96,445	2-Aug-96
1554	1554	GB_BA1:MTCY20G9	37218	Z77162	Mycobacterium tuberculosis H37Rv complete genome, segment 25/162.	Mycobacterium tuberculosis	59,429	17-Jun-98
1554	1554	GB_BA1:SCE7	16911	AL049819	Streptomyces coelicolor cosmid E7.	Streptomyces coelicolor	39,510	10-MAY-1999
1554	1554	GB_BA2:CGU31225	1817	U31225	Corynebacterium glutamicum L-proline: NADP+ 5-oxidoeductase (proC) gene, complete cds.	Corynebacterium glutamicum	97,749	2-Aug-96
1554	1554	GB_BA1:NG17PILA	1920	X13965	Neisseria gonorrhoeae pilA gene.	Neisseria gonorrhoeae	43,249	30-Sep-93
1554	1554	GB_HTG2:AC007984	129715	AC007984	Drosophila melanogaster chromosome 3 clone BACR05C10 (D781) RPCI-98 05.C.10 map 97D-97E strain y; cn bw sp. *** SEQUENCING IN PROGRESS ***; 87 unordered pieces.	Drosophila melanogaster	33,406	2-Aug-99
1554	1554	GB_BA1:MTCY20G9	37218	Z77162	Mycobacterium tuberculosis H37Rv complete genome, segment 25/162.	Mycobacterium tuberculosis	39,357	17-Jun-98
1554	1554	GB_BA1:U00018	42991	U00018	Mycobacterium leprae cosmid B2168.	Mycobacterium leprae	51,768	01-MAR-1994
1554	1554	GB_VI:HE1CG	152261	X14112	Herpes simplex virus (HSV) type 1 complete genome.	human herpesvirus 1	39,378	17-Apr-97
1554	1554	GB_PR3:AC005328	35414	AC005328	Homo sapiens chromosome 19, cosmid R26660, complete sequence.	Homo sapiens	39,922	28-Jul-98
1554	1554	GB_PR3:AC005545	43514	AC005545	Homo sapiens chromosome 19, cosmid R26634, complete sequence.	Homo sapiens	39,922	3-Sep-98
1554	1554	GB_PR3:AC005328	35414	AC005328	Homo sapiens chromosome 19, cosmid R26660, complete sequence.	Homo sapiens	34,911	28-Jul-98
1554	1554	GB_BA1:MTCY20G9	37218	Z77162	Mycobacterium tuberculosis H37Rv complete genome, segment 25/162.	Mycobacterium tuberculosis	54,940	17-Jun-98
1554	1554	GB_PR3:AC005328	35414	AC005328	Homo sapiens chromosome 19, cosmid R26660, complete sequence.	Homo sapiens	41,265	28-Jul-98
1554	1554	GB_PR3:AC005545	43514	AC005545	Homo sapiens chromosome 19, cosmid R26634, complete sequence.	Homo sapiens	41,265	3-Sep-98
1554	1554	GB_BA1:MLCL536	36224	Z99125	Mycobacterium leprae cosmid L536.	Mycobacterium leprae	37,723	04-DEC-1998
1554	1554	GB_BA1:U00013	35881	U00013	Mycobacterium leprae cosmid B1496.	Mycobacterium leprae	37,723	01-MAR-1994

Table 4 (continued)

rx02517	570	GB_BA1:MTV007	32806	AL021184	Mycobacterium tuberculosis H37Rv complete genome; segment 64/162.	Mycobacterium tuberculosis	61,335	17-Jun-98
		GB_BA1:MLCL536	36224	Z99125	Mycobacterium leprae cosmid L536.	Mycobacterium leprae	37,018	04-DEC-1998
		GB_BA1:U00013	35881	U00013	Mycobacterium leprae cosmid B1496.	Mycobacterium leprae	37,018	01-MAR-1994
rx02532	1170	GB_BA1:SCC22	22115	AL096839	Streptomyces coelicolor cosmid C22.	Streptomyces coelicolor	37,071	12-Jul-99
		GB_OV:AF137219	831	AF137219	Amia calva mixed lineage leukemia-like protein (Mli) gene, partial cds.	Amia calva	36,853	7-Sep-99
		GB_EST30:AI645057	301	AI645057	vs52a10.y1 Stratagene mouse Tcell 937311 Mus musculus cDNA clone IMAGE:1149882 5', mRNA sequence.	Mus musculus	41,860	29-Apr-99
		GB_EST20:AA822595	429	AA822595	vs52a10.r1 Stratagene mouse Tcell 937311 Mus musculus cDNA clone IMAGE:1149882 5', mRNA sequence.	Mus musculus	42,353	17-Feb-98
rx02536	879	GB_HTG2:AF130866	118874	AF130866	Homo sapiens chromosome 8 clone PAC 172N13 map 8q24, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	40,754	21-MAR-1999
		GB_HTG2:AF130866	118874	AF130866	Homo sapiens chromosome 8 clone PAC 172N13 map 8q24, *** SEQUENCING IN PROGRESS ***; in unordered pieces.	Homo sapiens	40,754	21-MAR-1999
		GB_PL1:ATT12J5	84499	AL035522	Arabidopsis thaliana DNA chromosome 4, BAC clone T12J5 (ESSAII project).	Arabidopsis thaliana	35,053	24-Feb-99
rx02550	1434	GB_BA1:MTCY279	9150	Z97991	Mycobacterium tuberculosis H37Rv complete genome; segment 17/162.	Mycobacterium tuberculosis	37,773	17-Jun-98
		GB_BA1:MSG81970C	39399	L78815	Mycobacterium leprae cosmid B1970 DNA sequence.	Mycobacterium leprae	39,024	15-Jun-96
rx02559	1026	GB_BA2:SC2H4	25970	AL031514	Streptomyces coelicolor cosmid 2H4.	Streptomyces coelicolor A3(2)	37,906	19-OCT-1999
		GB_BA1:MTV004	69350	AL009198	Mycobacterium tuberculosis H37Rv complete genome; segment 144/162.	Mycobacterium tuberculosis	47,358	18-Jun-98
		GB_PAT:128684	5100	I28684	Sequence 1 from patent US 5573915.	Unknown.	39,138	6-Feb-97
		GB_BA1:MTU27357	5100	U27357	Mycobacterium tuberculosis cyclopropane mycolic acid synthase (cma1) gene, complete cds.	Mycobacterium tuberculosis	39,138	26-Sep-95
rx02622	1683	GB_BA2:AE001780	11997	AE001780	Thermotoga maritima section 92 of 136 of the complete genome.	Thermotoga maritima	44,914	2-Jun-99
		GB_OV:AF064564	49254	AF064564	Fugu rubripes neurofibromatosis type 1 (NF1), A-kinase anchor protein (AKAP84), BAW protein (BAW), and WSB1 protein (WSB1) genes, complete cds.	Fugu rubripes	39,732	17-Aug-99
		GB_OV:AF064564	49254	AF064564	Fugu rubripes neurofibromatosis type 1 (NF1), A-kinase anchor protein (AKAP84), BAW protein (BAW), and WSB1 protein (WSB1) genes, complete cds.	Fugu rubripes	36,703	17-Aug-99
rx02623	714	GB_GSS5:AQ818728	444	AQ818728	HS_5268_A1_G09_SP6E RPCI-11 Human Male BAC Library Homo sapiens genomic clone Plate=844 Col=17 Row=M, genomic survey sequence.	Homo sapiens	38,801	26-Aug-99
		GB_HTG5:AC011083	198586	AC011083	Homo sapiens chromosome 9 clone RP11-111M7 map 9, WORKING DRAFT SEQUENCE, 51 unordered pieces.	Homo sapiens	35,714	19-Nov-99
		GB_GSS6:AQ826948	544	AQ826948	HS_5014_A2_C12_T7A RPCI-11 Human Male BAC Library Homo sapiens genomic clone Plate=590 Col=24 Row=E, genomic survey sequence.	Homo sapiens	39,146	27-Aug-99

Table 4 (continued)

rx02629	708	GB_VI:BRSMGP	462	M86652	Bovine respiratory syncytial virus membrane glycoprotein mRNA, complete cds.	Bovine respiratory syncytial 37,013 virus	28-Apr-93
		GB_VI:BRSMGP	462	M86652	Bovine respiratory syncytial virus membrane glycoprotein mRNA, complete cds.	Bovine respiratory syncytial 37,013 virus	28-Apr-93
rx02645	1953	GB_PAT:A45577	1925	A45577	Sequence 1 from Patent WO9519442.	Corynebacterium glutamicum	07-MAR-1997
		GB_PAT:A45581	1925	A45581	Sequence 5 from Patent WO9519442.	Corynebacterium glutamicum	07-MAR-1997
		GB_BA1:CORILVA	1925	L01508	Corynebacterium glutamicum threonine dehydratase (livA) gene, complete cds.	Corynebacterium glutamicum	26-Apr-93
rx02646	1392	GB_BA1:CORILVA	1925	L01508	Corynebacterium glutamicum threonine dehydratase (livA) gene, complete cds.	Corynebacterium glutamicum	26-Apr-93
		GB_PAT:A45585	1925	A45585	Sequence 9 from Patent WO9519442.	Corynebacterium glutamicum	07-MAR-1997
		GB_PAT:A45583	1925	A45583	Sequence 7 from Patent WO9519442.	Corynebacterium glutamicum	07-MAR-1997
rx02648	1326	GB_OV:ICTCNC	2049	M83111	Ictalurus punctatus cyclic nucleotide-gated channel RNA sequence.	Ictalurus punctatus	24-MAY-1993
		GB_EST11:AA265464	345	AA265464	mx91c06.r1 Soares mouse NML Mus musculus cDNA clone IMAGE:693706 5' mRNA sequence.	Mus musculus	20-MAR-1997
rx02653		GB_GS58:AQ006950	480	AQ006950	CIT-HSP-2294E14. TR CIT-HSP Homo sapiens genomic clone 2294E14, genomic survey sequence.	Homo sapiens	27-Jun-98
rx02687	1068	GB_BA1:CORPHEA	1088	M13774	C. glutamicum pheA gene encoding prephenate dehydratase, complete cds.	Corynebacterium glutamicum	26-Apr-93
		GB_PAT:E04483	948	E04483	DNA encoding prephenate dehydratase.	Corynebacterium glutamicum	29-Sep-97
		GB_PAT:E06110	948	E06110	DNA encoding prephenate dehydratase.	Corynebacterium glutamicum	29-Sep-97
rx02717	1005	GB_PL1:HVC4H	59748	Y14573	Hordeum vulgare DNA for chromosome 4H.	Hordeum vulgare	25-MAR-1999
		GB_PR2:HS310H5	29718	Z69705	Human DNA sequence from cosmid 310H5 from a contig from the tip of the short arm of chromosome 16, spanning 2Mb of 16p13.3. Contains EST and CpG island.	Homo sapiens	22-Nov-99
		GB_PR3:AC004754	39188	AC004754	Homo sapiens chromosome 16, cosmid clone RT286 (LANL), complete sequence.	Homo sapiens	28-MAY-1998
rx02754	1461	GB_HTG2:AC008223	130212	AC008223	Drosophila melanogaster chromosome 3 clone BACR16118 (D815) RPCI-98 16.1.18 map 95A-95A strain y, cn bw sp, *** SEQUENCING IN PROGRESS***, 101 unordered pieces.	Drosophila melanogaster	2-Aug-99

Table 4 (continued)

GB_HTG2:AC008223	130212	AC008223	Drosophila melanogaster chromosome 3 clone BACR16118 (D815) RPCI-98 16.1.18 map 95A-95A strain y; cn bw sp. *** SEQUENCING IN PROGRESS ***; 101 unordered pieces.	Drosophila melanogaster	32,757	2-Aug-99
GB_BA1:MTCY71	42729	Z92771	Mycobacterium tuberculosis H37Rv complete genome; segment 141/162.	Mycobacterium tuberculosis	37,838	10-Feb-99
GB_HTG5:AC011678	171967	AC011678	Homo sapiens clone 14_B_7. *** SEQUENCING IN PROGRESS ***; 20 unordered pieces.	Homo sapiens	35,331	5-Nov-99
GB_HTG5:AC011678	171967	AC011678	Homo sapiens clone 14_B_7. *** SEQUENCING IN PROGRESS ***; 20 unordered pieces.	Homo sapiens	33,807	5-Nov-99
GB_BA2:AF064070	23183	AF064070	Burkholderia pseudomallei putative dihydroorotase (pyrC) gene, partial cds; putative 1-acyl-sn-glycerol-3-phosphate acyltransferase (plsC); putative diadenosine tetraphosphatase (apaH); complete cds; type II O-antigen biosynthesis gene cluster, complete sequence; putative undecaprenyl phosphate N-acetylglucosaminyltransferase; and putative UDP-glucose 4-epimerase genes, complete cds; and putative galactosyl transferase gene, partial cds.	Burkholderia pseudomallei	36,929	20-Jan-99
GB_BA2:AF038651	4077	AF038651	Corynebacterium glutamicum dipeptide-binding protein (dcIAE) gene, partial cds; adenine phosphoribosyltransferase (apt) and GTP pyrophosphokinase (rel) genes, complete cds; and unknown gene	Corynebacterium glutamicum	99,852	14-Sep-98
GB_IN1:CELT1984	37121	U80438	Caenorhabditis elegans cosmid T19B4.	Caenorhabditis elegans	43,836	04-DEC-1996
GB_EST36:AV193572	360	AV193572	AV193572 Yuji Kohara unpublished cDNA: Strain N2 hermaphrodite embryo Caenorhabditis elegans cDNA clone yk618h8 5'; mRNA sequence.	Caenorhabditis elegans	48,588	22-Jul-99
GB_BA2:AF038651	4077	AF038651	Corynebacterium glutamicum dipeptide-binding protein (dcIAE) gene, partial cds; adenine phosphoribosyltransferase (apt) and GTP pyrophosphokinase (rel) genes, complete cds; and unknown gene.	Corynebacterium glutamicum	99,914	14-Sep-98
GB_BA1:MTCY227	35946	Z17724	Mycobacterium tuberculosis H37Rv complete genome; segment 114/162.	Mycobacterium tuberculosis	38,339	17-Jun-98
GB_BA1:U00011	40429	U00011	Mycobacterium leprae cosmid B1177.	Mycobacterium leprae	38,996	01-MAR-1994
GB_BA1:MTCY159	33818	Z83863	Mycobacterium tuberculosis H37Rv complete genome; segment 111/162.	Mycobacterium tuberculosis	37,640	17-Jun-98
GB_PR4:AC006581	172931	AC006581	Homo sapiens 12p21 BAC RPC111-259O18 (Roswell Park Cancer Institute Human BAC Library) complete sequence.	Homo sapiens	37,906	3-Jun-99
GB_PR4:AC006581	172931	AC006581	Homo sapiens 12p21 BAC RPC111-259O18 (Roswell Park Cancer Institute Human BAC Library) complete sequence.	Homo sapiens	35,280	3-Jun-99
GB_BA1:MTCY159	33818	Z83863	Mycobacterium tuberculosis H37Rv complete genome; segment 111/162.	Mycobacterium tuberculosis	39,765	17-Jun-98
GB_OV:CHKCEK2	3694	M35195	Chicken tyrosine kinase (cek2) mRNA, complete cds.	Gallus gallus	38,937	28-Apr-93
GB_BA1:MSASDASK	5037	Z17372	M. smegmatis asd, ask-alpha, and ask-beta genes.	Mycobacterium smegmatis	38,495	9-Aug-94
GB_EST24:AI223401	169	AI223401	q949g01.x1 Soares, testis, NHT Homo sapiens cDNA clone IMAGE:1838448 3' similar to WP.C25D7.8 CE08394.1; mRNA sequence.	Homo sapiens	40,828	27-OCT-1998

Exemplification

Example 1: Preparation of total genomic DNA of *Corynebacterium glutamicum* ATCC 13032

- 5 A culture of *Corynebacterium glutamicum* (ATCC 13032) was grown overnight at 30°C with vigorous shaking in BHI medium (Difco). The cells were harvested by centrifugation, the supernatant was discarded and the cells were resuspended in 5 ml buffer-I (5% of the original volume of the culture — all indicated volumes have been calculated for 100 ml of culture volume). Composition of buffer-I: 140.34 g/l sucrose,
- 10 2.46 g/l $\text{MgSO}_4 \times 7\text{H}_2\text{O}$, 10 ml/l KH_2PO_4 solution (100 g/l, adjusted to pH 6.7 with KOH), 50 ml/l M12 concentrate (10 g/l $(\text{NH}_4)_2\text{SO}_4$, 1 g/l NaCl, 2 g/l $\text{MgSO}_4 \times 7\text{H}_2\text{O}$, 0.2 g/l CaCl_2 , 0.5 g/l yeast extract (Difco), 10 ml/l trace-elements-mix (200 mg/l $\text{FeSO}_4 \times \text{H}_2\text{O}$, 10 mg/l $\text{ZnSO}_4 \times 7\text{H}_2\text{O}$, 3 mg/l $\text{MnCl}_2 \times 4\text{H}_2\text{O}$, 30 mg/l H_3BO_3 , 20 mg/l $\text{CoCl}_2 \times 6\text{H}_2\text{O}$, 1 mg/l $\text{NiCl}_2 \times 6\text{H}_2\text{O}$, 3 mg/l $\text{Na}_2\text{MoO}_4 \times 2\text{H}_2\text{O}$, 500 mg/l complexing agent
- 15 (EDTA or citric acid), 100 ml/l vitamins-mix (0.2 mg/l biotin, 0.2 mg/l folic acid, 20 mg/l p-amino benzoic acid, 20 mg/l riboflavin, 40 mg/l ca-panthothenate, 140 mg/l nicotinic acid, 40 mg/l pyridoxole hydrochloride, 200 mg/l myo-inositol). Lysozyme was added to the suspension to a final concentration of 2.5 mg/ml. After an approximately 4 h incubation at 37°C, the cell wall was degraded and the resulting
- 20 protoplasts are harvested by centrifugation. The pellet was washed once with 5 ml buffer-I and once with 5 ml TE-buffer (10 mM Tris-HCl, 1 mM EDTA, pH 8). The pellet was resuspended in 4 ml TE-buffer and 0.5 ml SDS solution (10%) and 0.5 ml NaCl solution (5 M) are added. After adding of proteinase K to a final concentration of 200 µg/ml, the suspension is incubated for ca.18 h at 37°C. The DNA was purified by
- 25 extraction with phenol, phenol-chloroform-isoamylalcohol and chloroform-isoamylalcohol using standard procedures. Then, the DNA was precipitated by adding 1/50 volume of 3 M sodium acetate and 2 volumes of ethanol, followed by a 30 min incubation at -20°C and a 30 min centrifugation at 12,000 rpm in a high speed centrifuge using a SS34 rotor (Sorvall). The DNA was dissolved in 1 ml TE-buffer containing 20
- 30 µg/ml RNaseA and dialysed at 4°C against 1000 ml TE-buffer for at least 3 hours. During this time, the buffer was exchanged 3 times. To aliquots of 0.4 ml of the dialysed DNA solution, 0.4 ml of 2 M LiCl and 0.8 ml of ethanol are added. After a 30

min incubation at -20°C, the DNA was collected by centrifugation (13,000 rpm, Biofuge Fresco, Heraeus, Hanau, Germany). The DNA pellet was dissolved in TE-buffer. DNA prepared by this procedure could be used for all purposes, including southern blotting or construction of genomic libraries.

5

Example 2: Construction of genomic libraries in *Escherichia coli* of *Corynebacterium glutamicum* ATCC13032.

Using DNA prepared as described in Example 1, cosmid and plasmid libraries were constructed according to known and well established methods (see e.g., Sambrook, J. et al. (1989) "Molecular Cloning : A Laboratory Manual", Cold Spring Harbor Laboratory Press, or Ausubel, F.M. et al. (1994) "Current Protocols in Molecular Biology", John Wiley & Sons.)

Any plasmid or cosmid could be used. Of particular use were the plasmids pBR322 (Sutcliffe, J.G. (1979) *Proc. Natl. Acad. Sci. USA*, 75:3737-3741); pACYC177 (Change & Cohen (1978) *J. Bacteriol* 134:1141-1156), plasmids of the pBS series (pBSSK+, pBSSK- and others; Stratagene, LaJolla, USA), or cosmids as SuperCos1 (Stratagene, LaJolla, USA) or Lorist6 (Gibson, T.J., Rosenthal A. and Waterson, R.H. (1987) *Gene* 53:283-286. Gene libraries specifically for use in *C. glutamicum* may be constructed using plasmid pSL109 (Lee, H.-S. and A. J. Sinskey (1994) *J. Microbiol. Biotechnol.* 4: 256-263).

20

Example 3: DNA Sequencing and Computational Functional Analysis

Genomic libraries as described in Example 2 were used for DNA sequencing according to standard methods, in particular by the chain termination method using ABI377 sequencing machines (see e.g., Fleischman, R.D. et al. (1995) "Whole-genome Random Sequencing and Assembly of Haemophilus Influenzae Rd., *Science*, 269:496-512). Sequencing primers with the following nucleotide sequences were used: 5'-GGAAACAGTATGACCATG-3' or 5'-GTAAAACGACGGCCAGT-3'.

25

Example 4: *In vivo* Mutagenesis

In vivo mutagenesis of *Corynebacterium glutamicum* can be performed by passage of plasmid (or other vector) DNA through *E. coli* or other microorganisms (e.g. *Bacillus* spp. or yeasts such as *Saccharomyces cerevisiae*) which are impaired in their capabilities to maintain

30

the integrity of their genetic information. Typical mutator strains have mutations in the genes for the DNA repair system (e.g., mutHLS, mutD, mutT, etc.; for reference, see Rupp, W.D. (1996) DNA repair mechanisms, in: *Escherichia coli* and *Salmonella*, p. 2277-2294, ASM: Washington.) Such strains are well known to those of ordinary skill in the art. The use of such strains is illustrated, for example, in Greener, A. and Callahan, M. (1994) *Strategies* 7: 32-34.

Example 5: DNA Transfer Between *Escherichia coli* and *Corynebacterium glutamicum*

Several *Corynebacterium* and *Brevibacterium* species contain endogenous plasmids (as e.g., pHM1519 or pBL1) which replicate autonomously (for review see, e.g., Martin, J.F. et al. (1987) *Biotechnology*, 5:137-146). Shuttle vectors for *Escherichia coli* and *Corynebacterium glutamicum* can be readily constructed by using standard vectors for *E. coli* (Sambrook, J. et al. (1989), "Molecular Cloning: A Laboratory Manual", Cold Spring Harbor Laboratory Press or Ausubel, F.M. et al. (1994) "Current Protocols in Molecular Biology", John Wiley & Sons) to which a origin or replication for and a suitable marker from *Corynebacterium glutamicum* is added. Such origins of replication are preferably taken from endogenous plasmids isolated from *Corynebacterium* and *Brevibacterium* species. Of particular use as transformation markers for these species are genes for kanamycin resistance (such as those derived from the Tn5 or Tn903 transposons) or chloramphenicol (Winnacker, E.L. (1987) "From Genes to Clones — Introduction to Gene Technology, VCH, Weinheim). There are numerous examples in the literature of the construction of a wide variety of shuttle vectors which replicate in both *E. coli* and *C. glutamicum*, and which can be used for several purposes, including gene over-expression (for reference, see e.g., Yoshihama, M. et al. (1985) *J. Bacteriol.* 162:591-597, Martin J.F. et al. (1987) *Biotechnology*, 5:137-146 and Eikmanns, B.J. et al. (1991) *Gene*, 102:93-98).

Using standard methods, it is possible to clone a gene of interest into one of the shuttle vectors described above and to introduce such a hybrid vectors into strains of *Corynebacterium glutamicum*. Transformation of *C. glutamicum* can be achieved by protoplast transformation (Kastsumata, R. et al. (1984) *J. Bacteriol.* 159:306-311), electroporation (Liebl, E. et al. (1989) *FEMS Microbiol. Letters*, 53:399-303) and in cases where special vectors are used, also by conjugation (as described e.g. in Schäfer, A et al.

(1990) *J. Bacteriol.* 172:1663-1666). It is also possible to transfer the shuttle vectors for *C. glutamicum* to *E. coli* by preparing plasmid DNA from *C. glutamicum* (using standard methods well-known in the art) and transforming it into *E. coli*. This transformation step can be performed using standard methods, but it is advantageous to use an *Mcr*-deficient

5 *E. coli* strain, such as NM522 (Gough & Murray (1983) *J. Mol. Biol.* 166:1-19).

Genes may be overexpressed in *C. glutamicum* strains using plasmids which comprise pCG1 (U.S. Patent No. 4,617,267) or fragments thereof, and optionally the gene for kanamycin resistance from TN903 (Grindley, N.D. and Joyce, C.M. (1980) *Proc. Natl. Acad. Sci. USA* 77(12): 7176-7180). In addition, genes may be

10 overexpressed in *C. glutamicum* strains using plasmid pSL109 (Lee, H.-S. and A. J. Sinskey (1994) *J. Microbiol. Biotechnol.* 4: 256-263).

Aside from the use of replicative plasmids, gene overexpression can also be achieved by integration into the genome. Genomic integration in *C. glutamicum* or other *Corynebacterium* or *Brevibacterium* species may be accomplished by well-known

15 methods, such as homologous recombination with genomic region(s), restriction endonuclease mediated integration (REMI) (see, *e.g.*, DE Patent 19823834), or through the use of transposons. It is also possible to modulate the activity of a gene of interest by modifying the regulatory regions (*e.g.*, a promoter, a repressor, and/or an enhancer) by sequence modification, insertion, or deletion using site-directed methods (such as

20 homologous recombination) or methods based on random events (such as transposon mutagenesis or REMI). Nucleic acid sequences which function as transcriptional terminators may also be inserted 3' to the coding region of one or more genes of the invention; such terminators are well-known in the art and are described, for example, in Winnacker, E.L. (1987) *From Genes to Clones -- Introduction to Gene Technology*. VCH:

25 Weinheim.

Example 6: Assessment of the Expression of the Mutant Protein

Observations of the activity of a mutated protein in a transformed host cell rely on the fact that the mutant protein is expressed in a similar fashion and in a similar quantity

30 to that of the wild-type protein. A useful method to ascertain the level of transcription of the mutant gene (an indicator of the amount of mRNA available for translation to the gene product) is to perform a Northern blot (for reference see, for example, Ausubel *et al.*

- (1988) Current Protocols in Molecular Biology, Wiley: New York), in which a primer designed to bind to the gene of interest is labeled with a detectable tag (usually radioactive or chemiluminescent), such that when the total RNA of a culture of the organism is extracted, run on gel, transferred to a stable matrix and incubated with this probe, the
- 5 binding and quantity of binding of the probe indicates the presence and also the quantity of mRNA for this gene. This information is evidence of the degree of transcription of the mutant gene. Total cellular RNA can be prepared from *Corynebacterium glutamicum* by several methods, all well-known in the art, such as that described in Bormann, E.R. *et al.* (1992) *Mol. Microbiol.* 6: 317-326.
- 10 To assess the presence or relative quantity of protein translated from this mRNA, standard techniques, such as a Western blot, may be employed (see, for example, Ausubel *et al.* (1988) Current Protocols in Molecular Biology, Wiley: New York). In this process, total cellular proteins are extracted, separated by gel electrophoresis, transferred to a matrix such as nitrocellulose, and incubated with a probe, such as an antibody, which
- 15 specifically binds to the desired protein. This probe is generally tagged with a chemiluminescent or colorimetric label which may be readily detected. The presence and quantity of label observed indicates the presence and quantity of the desired mutant protein present in the cell.
- 20 **Example 7: Growth of Genetically Modified *Corynebacterium glutamicum* — Media and Culture Conditions**
- Genetically modified *Corynebacteria* are cultured in synthetic or natural growth media. A number of different growth media for *Corynebacteria* are both well-known and readily available (Lieb *et al.* (1989) *Appl. Microbiol. Biotechnol.*, 32:205-210; von der
- 25 Osten *et al.* (1998) *Biotechnology Letters*, 11:11-16; Patent DE 4,120,867; Liebl (1992) "The Genus *Corynebacterium*, in: The Prokaryotes, Volume II, Balows, A. *et al.*, eds. Springer-Verlag). These media consist of one or more carbon sources, nitrogen sources, inorganic salts, vitamins and trace elements. Preferred carbon sources are sugars, such as mono-, di-, or polysaccharides. For example, glucose, fructose, mannose, galactose,
- 30 ribose, sorbose, ribulose, lactose, maltose, sucrose, raffinose, starch or cellulose serve as very good carbon sources. It is also possible to supply sugar to the media via complex compounds such as molasses or other by-products from sugar refinement. It can also be

advantageous to supply mixtures of different carbon sources. Other possible carbon sources are alcohols and organic acids, such as methanol, ethanol, acetic acid or lactic acid. Nitrogen sources are usually organic or inorganic nitrogen compounds, or materials which contain these compounds. Exemplary nitrogen sources include ammonia gas or
5 ammonia salts, such as NH_4Cl or $(\text{NH}_4)_2\text{SO}_4$, NH_4OH , nitrates, urea, amino acids or complex nitrogen sources like corn steep liquor, soy bean flour, soy bean protein, yeast extract, meat extract and others.

Inorganic salt compounds which may be included in the media include the chloride-, phosphorous- or sulfate- salts of calcium, magnesium, sodium, cobalt,
10 molybdenum, potassium, manganese, zinc, copper and iron. Chelating compounds can be added to the medium to keep the metal ions in solution. Particularly useful chelating compounds include dihydroxyphenols, like catechol or protocatechuate, or organic acids, such as citric acid. It is typical for the media to also contain other growth factors, such as vitamins or growth promoters, examples of which include biotin, riboflavin, thiamin, folic
15 acid, nicotinic acid, pantothenate and pyridoxin. Growth factors and salts frequently originate from complex media components such as yeast extract, molasses, corn steep liquor and others. The exact composition of the media compounds depends strongly on the immediate experiment and is individually decided for each specific case. Information about media optimization is available in the textbook "Applied Microbiol. Physiology, A
20 Practical Approach (*eds.* P.M. Rhodes, P.F. Stanbury, IRL Press (1997) pp. 53-73, ISBN 0 19 963577 3). It is also possible to select growth media from commercial suppliers, like standard 1 (Merck) or BHI (grain heart infusion, DIFCO) or others.

All medium components are sterilized, either by heat (20 minutes at 1.5 bar and 121°C) or by sterile filtration. The components can either be sterilized together or, if
25 necessary, separately. All media components can be present at the beginning of growth, or they can optionally be added continuously or batchwise.

Culture conditions are defined separately for each experiment. The temperature should be in a range between 15°C and 45°C. The temperature can be kept constant or can be altered during the experiment. The pH of the medium should be in the range of 5 to
30 8.5, preferably around 7.0, and can be maintained by the addition of buffers to the media. An exemplary buffer for this purpose is a potassium phosphate buffer. Synthetic buffers such as MOPS, HEPES, ACES and others can alternatively or simultaneously be used. It

is also possible to maintain a constant culture pH through the addition of NaOH or NH₄OH during growth. If complex medium components such as yeast extract are utilized, the necessity for additional buffers may be reduced, due to the fact that many complex compounds have high buffer capacities. If a fermentor is utilized for culturing the micro-organisms, the pH can also be controlled using gaseous ammonia.

The incubation time is usually in a range from several hours to several days. This time is selected in order to permit the maximal amount of product to accumulate in the broth. The disclosed growth experiments can be carried out in a variety of vessels, such as microtiter plates, glass tubes, glass flasks or glass or metal fermentors of different sizes.

10 For screening a large number of clones, the microorganisms should be cultured in microtiter plates, glass tubes or shake flasks, either with or without baffles. Preferably 100 ml shake flasks are used, filled with 10% (by volume) of the required growth medium. The flasks should be shaken on a rotary shaker (amplitude 25 mm) using a speed-range of 100 – 300 rpm. Evaporation losses can be diminished by the maintenance

15 of a humid atmosphere; alternatively, a mathematical correction for evaporation losses should be performed.

If genetically modified clones are tested, an unmodified control clone or a control clone containing the basic plasmid without any insert should also be tested. The medium is inoculated to an OD₆₀₀ of 0.5 – 1.5 using cells grown on agar plates, such as CM plates

20 (10 g/l glucose, 2,5 g/l NaCl, 2 g/l urea, 10 g/l polypeptone, 5 g/l yeast extract, 5 g/l meat extract, 22 g/l NaCl, 2 g/l urea, 10 g/l polypeptone, 5 g/l yeast extract, 5 g/l meat extract, 22 g/l agar, pH 6.8 with 2M NaOH) that had been incubated at 30°C. Inoculation of the media is accomplished by either introduction of a saline suspension of *C. glutamicum* cells from CM plates or addition of a liquid preculture of this bacterium.

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Example 8 – *In vitro* Analysis of the Function of Mutant Proteins

The determination of activities and kinetic parameters of enzymes is well established in the art. Experiments to determine the activity of any given altered enzyme must be tailored to the specific activity of the wild-type enzyme, which is well

30 within the ability of one of ordinary skill in the art. Overviews about enzymes in general, as well as specific details concerning structure, kinetics, principles, methods, applications and examples for the determination of many enzyme activities may be

- found, for example, in the following references: Dixon, M., and Webb, E.C., (1979) *Enzymes*. Longmans: London; Fersht, (1985) *Enzyme Structure and Mechanism*. Freeman: New York; Walsh, (1979) *Enzymatic Reaction Mechanisms*. Freeman: San Francisco; Price, N.C., Stevens, L. (1982) *Fundamentals of Enzymology*. Oxford Univ. Press: Oxford; Boyer, P.D., ed. (1983) *The Enzymes*, 3rd ed. Academic Press: New York; Bisswanger, H., (1994) *Enzymkinetik*, 2nd ed. VCH: Weinheim (ISBN 3527300325); Bergmeyer, H.U., Bergmeyer, J., Graßl, M., eds. (1983-1986) *Methods of Enzymatic Analysis*, 3rd ed., vol. I-XII, Verlag Chemie: Weinheim; and Ullmann's Encyclopedia of Industrial Chemistry (1987) vol. A9, "Enzymes". VCH: Weinheim, p. 352-363.

The activity of proteins which bind to DNA can be measured by several well-established methods, such as DNA band-shift assays (also called gel retardation assays). The effect of such proteins on the expression of other molecules can be measured using reporter gene assays (such as that described in Kolmar, H. *et al.* (1995) *EMBO J.* 14: 3895-3904 and references cited therein). Reporter gene test systems are well known and established for applications in both pro- and eukaryotic cells, using enzymes such as beta-galactosidase, green fluorescent protein, and several others.

The determination of activity of membrane-transport proteins can be performed according to techniques such as those described in Gennis, R.B. (1989) "Pores, Channels and Transporters", in *Biomembranes, Molecular Structure and Function*, Springer: Heidelberg, p. 85-137; 199-234; and 270-322.

Example 9: Analysis of Impact of Mutant Protein on the Production of the Desired Product

The effect of the genetic modification in *C. glutamicum* on production of a desired compound (such as an amino acid) can be assessed by growing the modified microorganism under suitable conditions (such as those described above) and analyzing the medium and/or the cellular component for increased production of the desired product (*i.e.*, an amino acid). Such analysis techniques are well known to one of ordinary skill in the art, and include spectroscopy, thin layer chromatography, staining methods of various kinds, enzymatic and microbiological methods, and analytical chromatography such as high performance liquid chromatography (see, for example,

- Ullman, Encyclopedia of Industrial Chemistry, vol. A2, p. 89-90 and p. 443-613, VCH: Weinheim (1985); Fallon, A. *et al.*, (1987) "Applications of HPLC in Biochemistry" in: Laboratory Techniques in Biochemistry and Molecular Biology, vol. 17; Rehm *et al.* (1993) Biotechnology, vol. 3, Chapter III: "Product recovery and purification", page 469-714, VCH: Weinheim; Belter, P.A. *et al.* (1988) Bioseparations: downstream processing for biotechnology, John Wiley and Sons; Kennedy, J.F. and Cabral, J.M.S. (1992) Recovery processes for biological materials, John Wiley and Sons; Shaciwitz, J.A. and Henry, J.D. (1988) Biochemical separations, in: Ulmann's Encyclopedia of Industrial Chemistry, vol. B3, Chapter 11, page 1-27, VCH: Weinheim; and Dechow, F.J. (1989) Separation and purification techniques in biotechnology, Noyes Publications.)

In addition to the measurement of the final product of fermentation, it is also possible to analyze other components of the metabolic pathways utilized for the production of the desired compound, such as intermediates and side-products, to determine the overall efficiency of production of the compound. Analysis methods include measurements of nutrient levels in the medium (*e.g.*, sugars, hydrocarbons, nitrogen sources, phosphate, and other ions), measurements of biomass composition and growth, analysis of the production of common metabolites of biosynthetic pathways, and measurement of gasses produced during fermentation. Standard methods for these measurements are outlined in Applied Microbial Physiology, A Practical Approach, P.M. Rhodes and P.F. Stanbury, eds., IRL Press, p. 103-129; 131-163; and 165-192 (ISBN: 0199635773) and references cited therein.

Example 10: Purification of the Desired Product from *C. glutamicum* Culture

Recovery of the desired product from the *C. glutamicum* cells or supernatant of the above-described culture can be performed by various methods well known in the art. If the desired product is not secreted from the cells, the cells can be harvested from the culture by low-speed centrifugation, the cells can be lysed by standard techniques, such as mechanical force or sonication. The cellular debris is removed by centrifugation, and the supernatant fraction containing the soluble proteins is retained for further purification of the desired compound. If the product is secreted from the *C. glutamicum*

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cells, then the cells are removed from the culture by low-speed centrifugation, and the supernate fraction is retained for further purification.

The supernatant fraction from either purification method is subjected to chromatography with a suitable resin, in which the desired molecule is either retained on
5 a chromatography resin while many of the impurities in the sample are not, or where the impurities are retained by the resin while the sample is not. Such chromatography steps may be repeated as necessary, using the same or different chromatography resins. One of ordinary skill in the art would be well-versed in the selection of appropriate chromatography resins and in their most efficacious application for a particular molecule
10 to be purified. The purified product may be concentrated by filtration or ultrafiltration, and stored at a temperature at which the stability of the product is maximized.

There are a wide array of purification methods known to the art and the preceding method of purification is not meant to be limiting. Such purification techniques are described, for example, in Bailey, J.E. & Ollis, D.F. *Biochemical*
15 *Engineering Fundamentals*, McGraw-Hill: New York (1986).

The identity and purity of the isolated compounds may be assessed by techniques standard in the art. These include high-performance liquid chromatography (HPLC), spectroscopic methods, staining methods, thin layer chromatography, NIRS, enzymatic assay, or microbiologically. Such analysis methods are reviewed in: Patek *et al.* (1994)
20 *Appl. Environ. Microbiol.* 60: 133-140; Malakhova *et al.* (1996) *Biotekhnologiya* 11: 27-32; and Schmidt *et al.* (1998) *Bioprocess Engineer.* 19: 67-70. *Ullmann's Encyclopedia of Industrial Chemistry*, (1996) vol. A27, VCH: Weinheim, p. 89-90, p. 521-540, p. 540-547, p. 559-566, 575-581 and p. 581-587; Michal, G. (1999) *Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology*, John Wiley and Sons; Fallon, A. *et al.*
25 (1987) *Applications of HPLC in Biochemistry in: Laboratory Techniques in Biochemistry and Molecular Biology*, vol. 17.

Example 11: Analysis of the Gene Sequences of the Invention

The comparison of sequences and determination of percent homology between
30 two sequences are art-known techniques, and can be accomplished using a mathematical algorithm, such as the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 87:2264-68, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA*

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90:5873-77. Such an algorithm is incorporated into the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to MP nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to MP protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, one of ordinary skill in the art will know how to optimize the parameters of the program (*e.g.*, XBLAST and NBLAST) for the specific sequence being analyzed.

Another example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Meyers and Miller ((1988) *Comput. Appl. Biosci.* 4: 11-17). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used. Additional algorithms for sequence analysis are known in the art, and include ADVANCE and ADAM. described in Torelli and Robotti (1994) *Comput. Appl. Biosci.* 10:3-5; and FASTA, described in Pearson and Lipman (1988) *P.N.A.S.* 85:2444-8.

The percent homology between two amino acid sequences can also be accomplished using the GAP program in the GCG software package (available at <http://www.gcg.com>), using either a Blosum 62 matrix or a PAM250 matrix, and a gap weight of 12, 10, 8, 6, or 4 and a length weight of 2, 3, or 4. The percent homology between two nucleic acid sequences can be accomplished using the GAP program in the GCG software package, using standard parameters, such as a gap weight of 50 and a length weight of 3.

A comparative analysis of the gene sequences of the invention with those present in Genbank has been performed using techniques known in the art (see, *e.g.*, Bexevanis and Ouellette, eds. (1998) *Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins.* John Wiley and Sons: New York). The gene sequences of the invention

were compared to genes present in Genbank in a three-step process. In a first step, a BLASTN analysis (*e.g.*, a local alignment analysis) was performed for each of the sequences of the invention against the nucleotide sequences present in Genbank, and the top 500 hits were retained for further analysis. A subsequent FASTA search (*e.g.*, a
5 combined local and global alignment analysis, in which limited regions of the sequences are aligned) was performed on these 500 hits. Each gene sequence of the invention was subsequently globally aligned to each of the top three FASTA hits, using the GAP program in the GCG software package (using standard parameters). In order to obtain correct results, the length of the sequences extracted from Genbank were adjusted to the
10 length of the query sequences by methods well-known in the art. The results of this analysis are set forth in Table 4. The resulting data is identical to that which would have been obtained had a GAP (global) analysis alone been performed on each of the genes of the invention in comparison with each of the references in Genbank, but required significantly reduced computational time as compared to such a database-wide GAP
15 (global) analysis. Sequences of the invention for which no alignments above the cutoff values were obtained are indicated on Table 4 by the absence of alignment information. It will further be understood by one of ordinary skill in the art that the GAP alignment homology percentages set forth in Table 4 under the heading "% homology (GAP)" are listed in the European numerical format, wherein a ',' represents a decimal point. For
20 example, a value of "40,345" in this column represents "40.345%".

Example 12: Construction and Operation of DNA Microarrays

The sequences of the invention may additionally be used in the construction and application of DNA microarrays (the design, methodology, and uses of DNA arrays are
25 well known in the art, and are described, for example, in Schena, M. *et al.* (1995) *Science* 270: 467-470; Wodicka, L. *et al.* (1997) *Nature Biotechnology* 15: 1359-1367; DeSaizieu, A. *et al.* (1998) *Nature Biotechnology* 16: 45-48; and DeRisi, J.L. *et al.* (1997) *Science* 278: 680-686).

DNA microarrays are solid or flexible supports consisting of nitrocellulose,
30 nylon, glass, silicone, or other materials. Nucleic acid molecules may be attached to the surface in an ordered manner. After appropriate labeling, other nucleic acids or nucleic acid mixtures can be hybridized to the immobilized nucleic acid molecules, and the label

may be used to monitor and measure the individual signal intensities of the hybridized molecules at defined regions. This methodology allows the simultaneous quantification of the relative or absolute amount of all or selected nucleic acids in the applied nucleic acid sample or mixture. DNA microarrays, therefore, permit an analysis of the
5 expression of multiple (as many as 6800 or more) nucleic acids in parallel (see, *e.g.*, Schena, M. (1996) *BioEssays* 18(5): 427-431).

The sequences of the invention may be used to design oligonucleotide primers which are able to amplify defined regions of one or more *C. glutamicum* genes by a nucleic acid amplification reaction such as the polymerase chain reaction. The choice
10 and design of the 5' or 3' oligonucleotide primers or of appropriate linkers allows the covalent attachment of the resulting PCR products to the surface of a support medium described above (and also described, for example, Schena, M. *et al.* (1995) *Science* 270: 467-470).

Nucleic acid microarrays may also be constructed by *in situ* oligonucleotide
15 synthesis as described by Wodicka, L. *et al.* (1997) *Nature Biotechnology* 15: 1359-1367. By photolithographic methods, precisely defined regions of the matrix are exposed to light. Protective groups which are photolabile are thereby activated and undergo nucleotide addition, whereas regions that are masked from light do not undergo any modification. Subsequent cycles of protection and light activation permit the
20 synthesis of different oligonucleotides at defined positions. Small, defined regions of the genes of the invention may be synthesized on microarrays by solid phase oligonucleotide synthesis.

The nucleic acid molecules of the invention present in a sample or mixture of nucleotides may be hybridized to the microarrays. These nucleic acid molecules can be
25 labeled according to standard methods. In brief, nucleic acid molecules (*e.g.*, mRNA molecules or DNA molecules) are labeled by the incorporation of isotopically or fluorescently labeled nucleotides, *e.g.*, during reverse transcription or DNA synthesis. Hybridization of labeled nucleic acids to microarrays is described (*e.g.*, in Schena, M. *et al.* (1995) *supra*; Wodicka, L. *et al.* (1997), *supra*; and DeSaizieu A. *et al.* (1998),
30 *supra*). The detection and quantification of the hybridized molecule are tailored to the specific incorporated label. Radioactive labels can be detected, for example, as

described in Schena, M. *et al.* (1995) *supra*) and fluorescent labels may be detected, for example, by the method of Shalon *et al.* (1996) *Genome Research* 6: 639-645).

The application of the sequences of the invention to DNA microarray technology, as described above, permits comparative analyses of different strains of *C. glutamicum* or other Corynebacteria. For example, studies of inter-strain variations based on individual transcript profiles and the identification of genes that are important for specific and/or desired strain properties such as pathogenicity, productivity and stress tolerance are facilitated by nucleic acid array methodologies. Also, comparisons of the profile of expression of genes of the invention during the course of a fermentation reaction are possible using nucleic acid array technology.

Example 13: Analysis of the Dynamics of Cellular Protein Populations (Proteomics)

The genes, compositions, and methods of the invention may be applied to study the interactions and dynamics of populations of proteins, termed 'proteomics'. Protein populations of interest include, but are not limited to, the total protein population of *C. glutamicum* (e.g., in comparison with the protein populations of other organisms), those proteins which are active under specific environmental or metabolic conditions (e.g., during fermentation, at high or low temperature, or at high or low pH), or those proteins which are active during specific phases of growth and development.

Protein populations can be analyzed by various well-known techniques, such as gel electrophoresis. Cellular proteins may be obtained, for example, by lysis or extraction, and may be separated from one another using a variety of electrophoretic techniques. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) separates proteins largely on the basis of their molecular weight. Isoelectric focusing polyacrylamide gel electrophoresis (IEF-PAGE) separates proteins by their isoelectric point (which reflects not only the amino acid sequence but also posttranslational modifications of the protein). Another, more preferred method of protein analysis is the consecutive combination of both IEF-PAGE and SDS-PAGE, known as 2-D-gel electrophoresis (described, for example, in Hermann *et al.* (1998) *Electrophoresis* 19: 3217-3221; Fountoulakis *et al.* (1998) *Electrophoresis* 19: 1193-1202; Langen *et al.* (1997) *Electrophoresis* 18: 1184-1192; Antelmann *et al.* (1997) *Electrophoresis* 18:

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1451-1463). Other separation techniques may also be utilized for protein separation, such as capillary gel electrophoresis; such techniques are well known in the art.

Proteins separated by these methodologies can be visualized by standard techniques, such as by staining or labeling. Suitable stains are known in the art, and
5 include Coomassie Brilliant Blue, silver stain, or fluorescent dyes such as Sypro Ruby (Molecular Probes). The inclusion of radioactively labeled amino acids or other protein precursors (*e.g.*, ^{35}S -methionine, ^{35}S -cysteine, ^{14}C -labelled amino acids, ^{15}N -amino acids, $^{15}\text{NO}_3$ or $^{15}\text{NH}_4^+$ or ^{13}C -labelled amino acids) in the medium of *C. glutamicum* permits the labeling of proteins from these cells prior to their separation. Similarly,
10 fluorescent labels may be employed. These labeled proteins can be extracted, isolated and separated according to the previously described techniques.

Proteins visualized by these techniques can be further analyzed by measuring the amount of dye or label used. The amount of a given protein can be determined quantitatively using, for example, optical methods and can be compared to the amount
15 of other proteins in the same gel or in other gels. Comparisons of proteins on gels can be made, for example, by optical comparison, by spectroscopy, by image scanning and analysis of gels, or through the use of photographic films and screens. Such techniques are well-known in the art.

To determine the identity of any given protein, direct sequencing or other
20 standard techniques may be employed. For example, N- and/or C-terminal amino acid sequencing (such as Edman degradation) may be used, as may mass spectrometry (in particular MALDI or ESI techniques (see, *e.g.*, Langen *et al.* (1997) *Electrophoresis* 18: 1184-1192)). The protein sequences provided herein can be used for the identification of *C. glutamicum* proteins by these techniques.

25 The information obtained by these methods can be used to compare patterns of protein presence, activity, or modification between different samples from various biological conditions (*e.g.*, different organisms, time points of fermentation, media conditions, or different biotopes, among others). Data obtained from such experiments alone, or in combination with other techniques, can be used for various applications,
30 such as to compare the behavior of various organisms in a given (*e.g.*, metabolic) situation, to increase the productivity of strains which produce fine chemicals or to increase the efficiency of the production of fine chemicals.

Equivalents

Those of ordinary skill in the art will recognize, or will be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the

5 following claims.

What is claimed:

1. An isolated nucleic acid molecule from *Corynebacterium glutamicum* encoding a
5 metabolic pathway protein, or a portion thereof, provided that the nucleic acid
molecule does not consist of any of the F-designated genes set forth in Table 1.
2. The isolated nucleic acid molecule of claim 1, wherein said metabolic pathway
protein is selected from the group consisting of proteins involved in the metabolism
10 of an amino acid, a vitamin, a cofactor, a nutraceutical, a nucleotide, a nucleoside, or
trehalose.
3. An isolated *Corynebacterium glutamicum* nucleic acid molecule selected from the
group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the
15 Sequence Listing, or a portion thereof, provided that the nucleic acid molecule does
not consist of any of the F-designated genes set forth in Table 1.
4. An isolated nucleic acid molecule which encodes a polypeptide sequence selected
from the group consisting of those sequences set forth as even-numbered SEQ ID
20 NOs of the Sequence Listing, provided that the nucleic acid molecule does not
consist of any of the F-designated genes set forth in Table 1.
5. An isolated nucleic acid molecule which encodes a naturally occurring allelic variant
of a polypeptide selected from the group of amino acid sequences consisting of those
25 sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing,
provided that the nucleic acid molecule does not consist of any of the F-designated
genes set forth in Table 1.
6. An isolated nucleic acid molecule comprising a nucleotide sequence which is at least
30 50% homologous to a nucleotide sequence selected from the group consisting of
those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, or

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a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.

7. An isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides
5 of a nucleic acid comprising a nucleotide sequence selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
- 10 8. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1-7 under stringent conditions.
9. An isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1-8 or a portion thereof and a nucleotide sequence encoding a heterologous
15 polypeptide.
10. A vector comprising the nucleic acid molecule of any one of claims 1-9.
11. The vector of claim 10, which is an expression vector.
20
12. A host cell transfected with the expression vector of claim 11.
13. The host cell of claim 12, wherein said cell is a microorganism.
- 25 14. The host cell of claim 13, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.
15. The host cell of claim 12, wherein the expression of said nucleic acid molecule results in the modulation in production of a fine chemical from said cell.
30
16. The host cell of claim 15, wherein said fine chemical is selected from the group consisting of: organic acids, nonproteinogenic amino acids, purine and pyrimidine

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bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

17. A method of producing a polypeptide comprising culturing the host cell of claim 12
5 in an appropriate culture medium to, thereby, produce the polypeptide.
18. An isolated metabolic pathway polypeptide from *Corynebacterium glutamicum*, or a portion thereof.
- 10 19. The protein of claim 18, wherein said polypeptide is selected from the group of metabolic pathway proteins which participate in the metabolism of an amino acid, a vitamin, a cofactor, a nutraceutical, a nucleotide, a nucleoside, or trehalose.
20. An isolated polypeptide comprising an amino acid sequence selected from the group
15 consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.
21. An isolated polypeptide comprising a naturally occurring allelic variant of a
20 polypeptide comprising an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, or a portion thereof, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.
- 25 22. The isolated polypeptide of any of claims 18-21, further comprising heterologous amino acid sequences.
23. An isolated polypeptide which is encoded by a nucleic acid molecule comprising a
30 nucleotide sequence which is at least 50% homologous to a nucleic acid selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated nucleic acid molecules set forth in Table 1.

24. An isolated polypeptide comprising an amino acid sequence which is at least 50% homologous to an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing,
5 provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.

25. A method for producing a fine chemical, comprising culturing a cell containing a vector of claim 12 such that the fine chemical is produced.

10

26. The method of claim 25, wherein said method further comprises the step of recovering the fine chemical from said culture.

27. The method of claim 25, wherein said method further comprises the step of
15 transfecting said cell with the vector of claim 11 to result in a cell containing said vector.

28. The method of claim 25, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.

20

29. The method of claim 25, wherein said cell is selected from the group consisting of:
Corynebacterium glutamicum, *Corynebacterium herculis*, *Corynebacterium lilium*,
Corynebacterium acetoacidophilum, *Corynebacterium acetoglutamicum*,
Corynebacterium acetophilum, *Corynebacterium ammoniagenes*, *Corynebacterium*
25 *fujiokense*, *Corynebacterium nitrilophilus*, *Brevibacterium ammoniagenes*,
Brevibacterium butanicum, *Brevibacterium divaricatum*, *Brevibacterium flavum*,
Brevibacterium healii, *Brevibacterium ketoglutamicum*, *Brevibacterium*
ketosoreductum, *Brevibacterium lactofermentum*, *Brevibacterium linens*,
Brevibacterium paraffinolyticum, and those strains set forth in Table 3.

30

30. The method of claim 25, wherein expression of the nucleic acid molecule from said vector results in modulation of production of said fine chemical.

31. The method of claim 25, wherein said fine chemical is selected from the group consisting of: organic acids, nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols,
5 carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

32. The method of claim 25, wherein said fine chemical is an amino acid.

33. The method of claim 32, wherein said amino acid is drawn from the group consisting
10 of: lysine, glutamate, glutamine, alanine, aspartate, glycine, serine, threonine, methionine, cysteine, valine, leucine, isoleucine, arginine, proline, histidine, tyrosine, phenylalanine, and tryptophan.

34. A method for producing a fine chemical, comprising culturing a cell whose genomic
15 DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims 1-9.

35. A method for diagnosing the presence or activity of *Corynebacterium diphtheriae* in a subject, comprising detecting the presence of one or more of SEQ ID NOs 1
20 through 1156 of the Sequence Listing in the subject, provided that the sequences are not or are not encoded by any of the F-designated sequences set forth in Table 1, thereby diagnosing the presence or activity of *Corynebacterium diphtheriae* in the subject.

25 36. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth as odd-numbered SEQ ID NOs of the Sequence Listing, wherein the nucleic acid molecule is disrupted.

37. A host cell comprising a nucleic acid molecule selected from the group consisting of
30 the nucleic acid molecules set forth as odd-numbered SEQ ID NOs in the Sequence Listing, wherein the nucleic acid molecule comprises one or more nucleic acid

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modifications from the sequence set forth as odd-numbered SEQ ID NOs of the Sequence Listing s.

38. A host cell comprising a nucleic acid molecule selected from the group consisting of
5 the nucleic acid molecules set forth as odd-numbered SEQ ID NOs of the Sequence Listing , wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.

10

SEQUENCE LISTING

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 <120> CORYNEBACTERIUM GLUTAMICUM GENES ENCODING
 METABOLIC PATHWAY PROTEINS
 <130> BGI-121CPPC
 <140>
 <141>
 <160> 1156

 <210> 1
 <211> 948
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (101)..(925)
 <223> RXA02229

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 aagccttgga gattttgggt ctacaatagc gaggggtgaat ttg acc atc ccc ttt 115
 Leu Thr Ile Pro Phe
 1 5

 gcc aaa ggc cac gcc acc gaa aac gac ttc atc atc atc ccc gat gag 163
 Ala Lys Gly His Ala Thr Glu Asn Asp Phe Ile Ile Ile Pro Asp Glu
 10 15 20

 gat gcg cgc cta gat tta act cca gaa atg gtg gtc acg ctg tgt gac 211
 Asp Ala Arg Leu Asp Leu Thr Pro Glu Met Val Val Thr Leu Cys Asp
 25 30 35

 cgc cgc gcc ggg atc ggt gct gat ggt atc ctc cgc gtg gtt aaa gct 259
 Arg Arg Ala Gly Ile Gly Ala Asp Gly Ile Leu Arg Val Val Lys Ala
 40 45 50

 gca gac gta gaa ggc tcc acg gtc gac cca tcg ctg tgg ttc atg gat 307
 Ala Asp Val Glu Gly Ser Thr Val Asp Pro Ser Leu Trp Phe Met Asp
 55 60 65

 tac cgc aac gcc gat gga tct ttg gct gaa atg tgc ggc aat ggt gtg 355
 Tyr Arg Asn Ala Asp Gly Ser Leu Ala Glu Met Cys Gly Asn Gly Val
 70 75 80 85

 cgc ctg ttc gcg cac tgg ctg tac tcc cgc ggt ctt gtt gat aat acg 403
 Arg Leu Phe Ala His Trp Leu Tyr Ser Arg Gly Leu Val Asp Asn Thr
 90 95 100

 agc ttt gat atc ggt acc cgc gcc ggt gtc cgc cac gtt gat att ttg 451
 Ser Phe Asp Ile Gly Thr Arg Ala Gly Val Arg His Val Asp Ile Leu
 105 110 115

 cag gca gat caa cat tct gcg cag gtc cgc gtt gat atg ggc atc cct 499
 Gln Ala Asp Gln His Ser Ala Gln Val Arg Val Asp Met Gly Ile Pro
 120 125 130

 gac gtc acg gga tta tcc acc tgc gac atc aac ggc caa gta ttc gct 547
 Asp Val Thr Gly Leu Ser Thr Cys Asp Ile Asn Gly Gln Val Phe Ala

135	140	145	
ggc ctt ggc gtt gat atg ggt aac cca cac cta gcg tgc gtt gtg ccg			595
Gly Leu Gly Val Asp Met Gly Asn Pro His Leu Ala Cys Val Val Pro			
150	155	160	165
ggc tta agt gcg tcg gct ctt gcc gat atg gaa ctg cgc gca cct acg			643
Gly Leu Ser Ala Ser Ala Leu Ala Asp Met Glu Leu Arg Ala Pro Thr			
	170	175	180
ttt gat cag gaa ttc ttc ccc cac ggt gtg aac gta gaa atc gtc aca			691
Phe Asp Gln Glu Phe Phe Pro His Gly Val Asn Val Glu Ile Val Thr			
	185	190	195
gaa tta gaa gat gac gca gta tcg atg cgc gtg tgg gaa cgc gga gtg			739
Glu Leu Glu Asp Asp Ala Val Ser Met Arg Val Trp Glu Arg Gly Val			
	200	205	210
ggc gaa acc cgc tcc tgt ggc acg gga acc gtt gct gca gcg tgt gct			787
Gly Glu Thr Arg Ser Cys Gly Thr Gly Thr Val Ala Ala Ala Cys Ala			
	215	220	225
gct tta gct gat gct gga ttg gga gaa ggc aca gct aaa gtg tgc gtt			835
Ala Leu Ala Asp Ala Gly Leu Gly Glu Gly Thr Ala Lys Val Cys Val			
	230	235	240
cca cgt ggg gaa gta gaa gtc cag atc ttt gac gac ggc tcc aca ctc			883
Pro Arg Gly Glu Val Glu Val Gln Ile Phe Asp Asp Gly Ser Thr Leu			
	250	255	260
acc ggc cca agc gcc atc atc gca ctc ggt gag gtg cag atc			925
Thr Gly Pro Ser Ala Ile Ile Ala Leu Gly Glu Val Gln Ile			
	265	270	275
taagattcgc gattgtagtt cgg			948

<210> 2

<211> 275

<212> PRT

<213> Corynebacterium glutamicum

<400> 2

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 1 5 10 15

Ile Ile Pro Asp Glu Asp Ala Arg Leu Asp Leu Thr Pro Glu Met Val
 20 25 30

Val Thr Leu Cys Asp Arg Arg Ala Gly Ile Gly Ala Asp Gly Ile Leu
 35 40 45

Arg Val Val Lys Ala Ala Asp Val Glu Gly Ser Thr Val Asp Pro Ser
 50 55 60

Leu Trp Phe Met Asp Tyr Arg Asn Ala Asp Gly Ser Leu Ala Glu Met
 65 70 75 80

Cys Gly Asn Gly Val Arg Leu Phe Ala His Trp Leu Tyr Ser Arg Gly
 85 90 95

Leu Val Asp Asn Thr Ser Phe Asp Ile Gly Thr Arg Ala Gly Val Arg
 100 105 110
 His Val Asp Ile Leu Gln Ala Asp Gln His Ser Ala Gln Val Arg Val
 115 120 125
 Asp Met Gly Ile Pro Asp Val Thr Gly Leu Ser Thr Cys Asp Ile Asn
 130 135 140
 Gly Gln Val Phe Ala Gly Leu Gly Val Asp Met Gly Asn Pro His Leu
 145 150 155 160
 Ala Cys Val Val Pro Gly Leu Ser Ala Ser Ala Leu Ala Asp Met Glu
 165 170 175
 Leu Arg Ala Pro Thr Phe Asp Gln Glu Phe Phe Pro His Gly Val Asn
 180 185 190
 Val Glu Ile Val Thr Glu Leu Glu Asp Asp Ala Val Ser Met Arg Val
 195 200 205
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 Ala Ala Ala Cys Ala Ala Leu Ala Asp Ala Gly Leu Gly Glu Gly Thr
 225 230 235 240
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 Lys Glu Glu Glu Lys Arg Ala Phe Asp Asn Asp Arg Ala His Val Phe
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His Ser Trp Ser Ala Gln Asp Lys Ile Ser Pro Lys Val Trp Ala Ala	
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Ala Glu Gly Ser Thr Leu Tyr Asp Phe Asp Gly Asn Ala Phe Ile Asp	
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Met Gly Ser Gln Leu Val Ser Ala Asn Leu Gly His Asn Asn Pro Arg	
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Leu Val Glu Ala Ile Gln Arg Gln Ala Ala Arg Leu Thr Asn Ile Asn	
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Pro Ala Phe Gly Asn Asp Val Arg Ser Asp Val Ala Ala Lys Ile Val	
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Arg Asn Lys Ile Leu Ser Ala Tyr Arg Ser Tyr His Gly Ala Thr Gly	
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Ser Ala Met Met Leu Thr Gly Glu His Arg Arg Leu Gly Asn Pro Thr	
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Thr Asp Pro Asp Ile Tyr His Phe Trp Ala Pro Phe Leu His His Ser	
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Ser Phe Phe Ala Thr Thr Gln Glu Glu Cys Glu Arg Ala Leu Lys	
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215 220 225	
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Ala Gly Tyr Leu Asn Gly Val Arg Glu Leu Cys Asn Lys His Gly Ile	
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Leu Phe Ile Ala Asp Glu Val Met Val Gly Phe Gly Arg Thr Gly Lys	
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 1363
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          35          40          45

Lys Val Trp Ala Ala Ala Glu Gly Ser Thr Leu Tyr Asp Phe Asp Gly
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Asn Ala Phe Ile Asp Met Gly Ser Gln Leu Val Ser Ala Asn Leu Gly
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His Asn Asn Pro Arg Leu Val Glu Ala Ile Gln Arg Gln Ala Ala Arg
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Leu Thr Asn Ile Asn Pro Ala Phe Gly Asn Asp Val Arg Ser Asp Val
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Ala Ala Lys Ile Val Ser Met Ala Arg Gly Glu Phe Ser His Val Phe
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Phe Thr Asn Gly Gly Ala Asp Ala Ile Glu His Ser Ile Arg Met Ala
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Arg Leu His Thr Gly Arg Asn Lys Ile Leu Ser Ala Tyr Arg Ser Tyr
          145          150          155          160

His Gly Ala Thr Gly Ser Ala Met Met Leu Thr Gly Glu His Arg Arg
          165          170          175

Leu Gly Asn Pro Thr Thr Asp Pro Asp Ile Tyr His Phe Trp Ala Pro
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Phe Leu His His Ser Ser Phe Phe Ala Thr Thr Gln Glu Glu Glu Cys
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Glu Arg Ala Leu Lys His Leu Glu Asp Val Ile Ala Phe Glu Gly Ala
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Gly Met Ile Ala Ala Ile Val Leu Glu Pro Val Val Gly Ser Ser Gly
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Ile Ile Leu Pro Pro Ala Gly Tyr Leu Asn Gly Val Arg Glu Leu Cys
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Asn Lys His Gly Ile Leu Phe Ile Ala Asp Glu Val Met Val Gly Phe
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Gly Arg Thr Gly Lys Leu Phe Ala Tyr Glu His Ala Gly Asp Asp Phe
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Gln Pro Asp Met Ile Thr Phe Ala Lys Gly Val Asn Ala Gly Tyr Ala
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Val Ala Pro Ala Lys Ala Ala Leu Glu Ile Tyr Ala Glu Gly Glu Ile
 340 345 350

Ile Pro Arg Val Ala Arg Leu Gly Ala Glu Leu Ile Glu Pro Arg Leu
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Arg Glu Leu Ala Glu Glu Asn Val Ala Ile Ala Asp Val Arg Gly Ile
 370 375 380

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Gly Asn Arg Phe His Ile Ala Pro Pro Leu Thr Thr Thr Asp Asp Glu
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 Lys Glu Glu Glu Lys Arg Ala Phe Asp Asn Asp Arg Ala His Val Phe
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cac tcc tgg tcc gcg cag gac aaa atc agc ccc aaa gta tgg gca gct 259
 His Ser Trp Ser Ala Gln Asp Lys Ile Ser Pro Lys Val Trp Ala Ala
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 Pro Ala Phe Gly Asn Asp Val Arg Ser Asp Val Ala Ala Lys Ile Val
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 Ala Asp Ala Ile Glu His Ser Ile Arg Met Ala Arg Leu His Thr Gly
 135 140 145

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 Arg Asn Lys Ile Leu Ser Ala Tyr Arg Ser Tyr His Gly Ala Thr Gly
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 Ser Ala Met Met Leu Thr Gly Glu His Arg Arg Leu Gly Asn Pro Thr
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 His Leu Glu Asp Val Ile Ala Phe Glu Gly Ala Gly Met Ile Ala Ala
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 Ile Val Leu Glu Pro Val Val Gly Ser Ser Gly Ile Ile Leu Pro Pro
 230 235 240 245

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 Ala Gly Tyr Leu Asn Gly Val Arg Glu Leu Cys Asn Lys His Gly Ile
 250 255 260

ctc ttc atc gcc gac gaa gtc atg gtc gga ttc gga cgc acc gga aaa 931
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 265 270 275

ctg ttt gct tac gag cat gct ggc gac gat ttc cag cca gac atg atc 979
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Thr Phe Ala Lys Gly Val Asn Ala Gly Tyr Ala Pro Leu Gly Gly Ile
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1075

Val Met Thr Gln Ser Ile Arg Asp Thr Phe Gly Ser Glu Ala Tyr Ser
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1123

Gly Gly Leu Thr Tyr Ser Gly His Pro Leu Ala Val Ala Pro Ala Lys
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1267

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Asn Ala Phe Ile Asp Met Gly Ser Gln Leu Val Ser Ala Asn Leu Gly
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His Asn Asn Pro Arg Leu Val Glu Ala Ile Gln Arg Gln Ala Ala Arg
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 Leu Thr Asn Ile Asn Pro Ala Phe Gly Asn Asp Val Arg Ser Asp Val
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 Ala Ala Lys Ile Val Ser Met Ala Arg Gly Glu Phe Ser His Val Phe
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 Phe Thr Asn Gly Gly Ala Asp Ala Ile Glu His Ser Ile Arg Met Ala
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 Arg Leu His Thr Gly Arg Asn Lys Ile Leu Ser Ala Tyr Arg Ser Tyr
 145 150 155 160
 His Gly Ala Thr Gly Ser Ala Met Met Leu Thr Gly Glu His Arg Arg
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 Phe Leu His His Ser Ser Phe Phe Ala Thr Thr Gln Glu Glu Glu Cys
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 Glu Arg Ala Leu Lys His Leu Glu Asp Val Ile Ala Phe Glu Gly Ala
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 Ile Ile Leu Pro Pro Ala Gly Tyr Leu Asn Gly Val Arg Glu Leu Cys
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 Gly Arg Thr Gly Lys Leu Phe Ala Tyr Glu His Ala Gly Asp Asp Phe
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 Gln Pro Asp Met Ile Thr Phe Ala Lys Gly Val Asn Ala Gly Tyr Ala
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 Val Ala Pro Ala Lys Ala Ala Leu Glu Ile Tyr Ala Glu Gly Glu Ile
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 Ile Pro Arg Val Ala Arg Leu Gly Ala Glu Leu Ile Glu Pro Arg Leu
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Gln Phe Arg Phe Asn Ala Asp Ala Arg Pro Ile Pro Asp Ala Val Glu																		
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135 140 145																		
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 35 40 45

Leu Thr Val Trp Val Thr Leu Thr Val Val Gly Ala Ala Ala Leu Leu
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 65 70 75 80

Tyr Leu Ser Phe Ile Gly Tyr Lys Leu Leu Arg Ser Ala Ser Arg Glu
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Leu Ile Asp Ala Arg Gln Phe Arg Phe Asn Ala Asp Ala Arg Pro Ile
 100 105 110

Pro Asp Ala Val Glu Ala Leu Gly Thr Arg Thr Gln Val Tyr Arg Gln
 115 120 125

Gly Leu Ala Thr Asn Leu Ser Asn Pro Lys Val Val Met Tyr Phe Ala
 130 135 140

Ala Ile Leu Ala Pro Leu Met Pro Ala His Pro Ser Pro Val Leu Ala
 145 150 155 160

Phe Ser Ile Ile Val Ala Ile Leu Val Gln Thr Phe Val Thr Phe Ser
 165 170 175

Ala Val Cys Leu Ile Val Ser Thr Glu Arg Val Arg Lys Ala Met Leu
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 Leu Leu Leu Gly Gly
 1 5

aac cct gcc gag atc gac cag gtt tta ggt ggc gat caa acc cag atc 163
 Asn Pro Ala Glu Ile Asp Gln Val Leu Gly Gly Asp Gln Thr Gln Ile
 10 15 20

gag tct gga gag tcc acc gga gcc ggc gac ttt gat cac tgc caa acc 211
 Glu Ser Gly Glu Ser Thr Gly Ala Gly Asp Phe Asp His Cys Gln Thr
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 Gly Ala Asp Ala Asn Ala Ser Asp Asp Cys Arg Leu Tyr Tyr Thr Ser
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 Gln Phe Gly Ala Glu Asn Ala Pro Leu Ala Gln Met Tyr Ile Val Ala
 120 125 130

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 His Glu Tyr Gly His His Val Gln Asn Leu Glu Gly Thr Leu Gly Leu
 135 140 145

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Ser Asn Tyr Asn Asp Pro Gly Ala Asp Ser Asn Ala Val Lys Ile Glu
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 185 190 195

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<213> Corynebacterium glutamicum

<400> 10

Leu Leu Leu Gly Gly Asn Pro Ala Glu Ile Asp Gln Val Leu Gly Gly
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Asp Gln Thr Gln Ile Glu Ser Gly Glu Ser Thr Gly Ala Gly Asp Phe
 20 25 30

Asp His Cys Gln Thr Gly Ala Asp Ala Asn Ala Ser Asp Asp Cys Arg
 35 40 45

Leu Tyr Tyr Thr Ser Phe Ser Val Asn Glu Met Trp Gln Thr Leu Leu
 50 55 60

Pro Ala Gln Ala Gly Ile Glu Tyr Thr Glu Pro Thr Leu Thr Leu Phe
 65 70 75 80

Lys Asn Ser Thr Gln Thr Gly Cys Gly Phe Ala Ser Ala Ser Thr Gly
 85 90 95

Pro Phe Tyr Cys Pro Ser Asp Gln Asp Ala Tyr Phe Asp Leu Thr Phe
 100 105 110

Phe Asp Gln Met Arg Gln Phe Gly Ala Glu Asn Ala Pro Leu Ala Gln
 115 120 125

Met Tyr Ile Val Ala His Glu Tyr Gly His His Val Gln Asn Leu Glu

130	135	140
Gly Thr Leu Gly Leu Ser Asn Tyr Asn Asp Pro Gly Ala Asp Ser Asn		
145	150	155 160
Ala Val Lys Ile Glu Leu Gln Ala Asp Cys Tyr Ala Gly Ile Trp Ala		
	165	170 175
Asn His Ser Ser Glu Gly Pro Asp Pro Leu Leu Gln Pro Ile Thr Glu		
	180	185 190
Ser Glu Leu Asp Ser Ala Leu Leu Ala Ala Ser Ala Val Gly Asp Asp		
	195	200 205
Asn Ile Gln Gln Arg Ser Gly Gly Asp Val Asn Pro Glu Ser Trp Thr		
	210	215 220
His Gly Ser Ser Gln Gln Arg Lys Asp Ala Phe Leu Ala Gly Tyr Asn		
	225	230 235 240
Thr Gly Gln Met Ser Ala Cys Asp Phe Leu Gly Arg Gly Val Tyr Asn		
	245	250 255

Asp Ala

<210> 11
 <211> 771
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (101)..(748)
 <223> RXC01207

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 Val Ser Arg Ile Tyr
 1 5
 gac tgt gcc gac caa gac tcc cgt gca gca ggc cta aag gcg gct gtc 163
 Asp Cys Ala Asp Gln Asp Ser Arg Ala Ala Gly Leu Lys Ala Ala Val
 10 15 20
 gat gca gtc aaa gcc ggt cag ctc gtt gtc ctt ccc acg gat acc ctt 211
 Asp Ala Val Lys Ala Gly Gln Leu Val Val Leu Pro Thr Asp Thr Leu
 25 30 35
 tat gga ctc ggc tgc gac gct ttc aac aac gag gca gta gcc aac ctt 259
 Tyr Gly Leu Gly Cys Asp Ala Phe Asn Asn Glu Ala Val Ala Asn Leu
 40 45 50
 ctg gcc acc aaa cac cgt ggc ccc gat atg ccc gtt cca gtg ctc gtc 307
 Leu Ala Thr Lys His Arg Gly Pro Asp Met Pro Val Pro Val Leu Val
 55 60 65
 ggc agc tgg gac acc att caa gga ctt gtg cac tcc tat tct gcg cag 355

[illegible]

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<210> 12
<211> 216
<212> PRT
<213> Corynebacterium glutamicum
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<400> 12
Val Ser Arg Ile Tyr Asp Cys Ala Asp Gln Asp Ser Arg Ala Ala Gly
  1                               5                10                15
Leu Lys Ala Ala Val Asp Ala Val Lys Ala Gly Gln Leu Val Val Leu
      20                        25                        30
Pro Thr Asp Thr Leu Tyr Gly Leu Gly Cys Asp Ala Phe Asn Asn Glu
      35                        40                        45
Ala Val Ala Asn Leu Leu Ala Thr Lys His Arg Gly Pro Asp Met Pro
      50                        55                        60
Val Pro Val Leu Val Gly Ser Trp Asp Thr Ile Gln Gly Leu Val His
      65                        70                        75                        80

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Ser	Tyr	Ser	Ala	Gln	Ala	Lys	Ala	Leu	Val	Glu	Ala	Phe	Trp	Pro	Gly
				85					90					95	
Gly	Leu	Ser	Ile	Ile	Val	Pro	Gln	Ala	Pro	Ser	Leu	Pro	Trp	Asn	Leu
			100					105					110		
Gly	Asp	Thr	Arg	Gly	Thr	Val	Met	Leu	Arg	Met	Pro	Leu	His	Pro	Val
		115					120					125			
Ala	Ile	Glu	Leu	Leu	Arg	Gln	Thr	Gly	Pro	Met	Ala	Val	Ser	Ser	Ala
	130					135					140				
Asn	Ile	Ser	Gly	His	Thr	Pro	Pro	Thr	Thr	Val	Leu	Glu	Ala	Arg	Gln
145					150					155					160
Gln	Leu	Asn	Gln	Asn	Val	Ala	Val	Tyr	Leu	Asp	Gly	Gly	Glu	Cys	Ala
			165						170					175	
Leu	Ala	Thr	Pro	Ser	Thr	Ile	Val	Asp	Ile	Ser	Gly	Pro	Ala	Pro	Lys
			180					185					190		
Ile	Leu	Arg	Glu	Gly	Ala	Ile	Ser	Ala	Glu	Arg	Val	Gly	Glu	Val	Leu
		195					200					205			
Gly	Val	Ser	Ala	Glu	Ser	Leu	Arg								
	210					215									

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<210> 13
<211> 1026
<212> DNA
<213> Corynebacterium glutamicum
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<220>
<221> CDS
<222> (101) .. (1003)
<223> RXC00657
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tgta	acgcag	gatt	caacaa	tcaat	gaaag	gtc	gacc	gac	atg	agc	act	gaa	gac				115		
												Met	Ser	Thr	Glu	Asp			
												1				5			
att	gtc	gtc	gta	gca	gta	gat	ggc	tgc	gac	gcc	tca	aaa	caa	gct	gtt			163	
Ile	Val	Val	Val	Ala	Val	Asp	Gly	Ser	Asp	Ala	Ser	Lys	Gln	Ala	Val				
				10					15					20					
cgg	tgg	gct	gca	aat	acc	gcc	aac	aaa	cgt	ggc	att	cca	ctt	cgc	ttg			211	
Arg	Trp	Ala	Ala	Asn	Thr	Ala	Asn	Lys	Arg	Gly	Ile	Pro	Leu	Arg	Leu				
				25					30					35					
gct	tcc	agc	tac	acc	atg	cct	cag	ttc	ctc	tac	gca	gag	gga	atg	gtt			259	
Ala	Ser	Ser	Tyr	Thr	Met	Pro	Gln	Phe	Leu	Tyr	Ala	Glu	Gly	Met	Val				
				40					45					50					
cca	cca	caa	gag	ctt	ttc	gat	gac	ctc	cag	gcc	gaa	gcc	ctg	gaa	aag			307	
Pro	Pro	Gln	Glu	Leu	Phe	Asp	Asp	Leu	Gln	Ala	Glu	Ala	Leu	Glu	Lys				
			55				60				65								

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att aac gaa gcc cgt gac atc gcc cat gag gta gcg cca gaa atc aag 355
Ile Asn Glu Ala Arg Asp Ile Ala His Glu Val Ala Pro Glu Ile Lys
70 75 80 85

atc ggg cac acc atc gct gaa ggc agt ccc atc gac atg ctg ttg gaa 403
Ile Gly His Thr Ile Ala Glu Gly Ser Pro Ile Asp Met Leu Leu Glu
90 95 100

atg tct ccc gat gcc aca atg atc gtc atg ggt tcc cgc gga ctc ggc 451
Met Ser Pro Asp Ala Thr Met Ile Val Met Gly Ser Arg Gly Leu Gly
105 110 115

gga ctc tcc gga atg gtc atg ggc tcc gtc tcc ggt gca gtg gtc agc 499
Gly Leu Ser Gly Met Val Met Gly Ser Val Ser Gly Ala Val Val Ser
120 125 130

cac gca aag tgt cca gtc gtt gtt gtc cgt gaa gac agc gca gtc aac 547
His Ala Lys Cys Pro Val Val Val Val Arg Glu Asp Ser Ala Val Asn
135 140 145

gaa gac agc aag tac ggc cca gtc gtc gtc ggt gtg gat ggc tcc gaa 595
Glu Asp Ser Lys Tyr Gly Pro Val Val Val Gly Val Asp Gly Ser Glu
150 155 160 165

gtc tcc caa cag gca acc gaa tac gca ttt gcg gaa gct gaa gct cgt 643
Val Ser Gln Gln Ala Thr Glu Tyr Ala Phe Ala Glu Ala Glu Ala Arg
170 175 180

ggc gcc gaa ctc gtt gca gtt cac acc tgg atg gac atg cag gta cag 691
Gly Ala Glu Leu Val Ala Val His Thr Trp Met Asp Met Gln Val Gln
185 190 195

gca tca ctt gca ggt ctt gca gct gct caa cag cag tgg gat gaa gtg 739
Ala Ser Leu Ala Gly Leu Ala Ala Gln Gln Gln Trp Asp Glu Val
200 205 210

gaa cgt cag caa acc gac atg ctg atc gaa cgc ctc gca cca ctg gtg 787
Glu Arg Gln Gln Thr Asp Met Leu Ile Glu Arg Leu Ala Pro Leu Val
215 220 225

gaa aag tac cca agt gta acc gtc aag aag atc atc acc cgt gac cgc 835
Glu Lys Tyr Pro Ser Val Thr Val Lys Lys Ile Ile Thr Arg Asp Arg
230 235 240 245

cca gtt cgc gca ctt gca gaa gca tct gaa aac gcg cag ctc cta gtc 883
Pro Val Arg Ala Leu Ala Glu Ala Ser Glu Asn Ala Gln Leu Leu Val
250 255 260

gtt ggt tcc cat ggt cgt ggc gga ttt aag ggc atg ctc ctt ggc tcc 931
Val Gly Ser His Gly Arg Gly Gly Phe Lys Gly Met Leu Leu Gly Ser
265 270 275

acc tcc cgc gca ctg ctg caa tcc gca ccg tgc cca atg atg gtg gtt 979
Thr Ser Arg Ala Leu Leu Gln Ser Ala Pro Cys Pro Met Met Val Val
280 285 290

cgc cca cct gag aag att aag aag tagttttcttt taagtttcga tgc
1026
Arg Pro Pro Glu Lys Ile Lys Lys
295 300

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<210> 14

<211> 301

<212> PRT

<213> *Corynebacterium glutamicum*

<400> 14

Met Ser Thr Glu Asp Ile Val Val Val Ala Val Asp Gly Ser Asp Ala
 1 5 10 15

Ser Lys Gln Ala Val Arg Trp Ala Ala Asn Thr Ala Asn Lys Arg Gly
 20 25 30

Ile Pro Leu Arg Leu Ala Ser Ser Tyr Thr Met Pro Gln Phe Leu Tyr
 35 40 45

Ala Glu Gly Met Val Pro Pro Gln Glu Leu Phe Asp Asp Leu Gln Ala
 50 55 60

Glu Ala Leu Glu Lys Ile Asn Glu Ala Arg Asp Ile Ala His Glu Val
 65 70 75 80

Ala Pro Glu Ile Lys Ile Gly His Thr Ile Ala Glu Gly Ser Pro Ile
 85 90 95

Asp Met Leu Leu Glu Met Ser Pro Asp Ala Thr Met Ile Val Met Gly
 100 105 110

Ser Arg Gly Leu Gly Gly Leu Ser Gly Met Val Met Gly Ser Val Ser
 115 120 125

Gly Ala Val Val Ser His Ala Lys Cys Pro Val Val Val Val Arg Glu
 130 135 140

Asp Ser Ala Val Asn Glu Asp Ser Lys Tyr Gly Pro Val Val Val Gly
 145 150 155 160

Val Asp Gly Ser Glu Val Ser Gln Gln Ala Thr Glu Tyr Ala Phe Ala
 165 170 175

Glu Ala Glu Ala Arg Gly Ala Glu Leu Val Ala Val His Thr Trp Met
 180 185 190

Asp Met Gln Val Gln Ala Ser Leu Ala Gly Leu Ala Ala Ala Gln Gln
 195 200 205

Gln Trp Asp Glu Val Glu Arg Gln Gln Thr Asp Met Leu Ile Glu Arg
 210 215 220

Leu Ala Pro Leu Val Glu Lys Tyr Pro Ser Val Thr Val Lys Lys Ile
 225 230 235 240

Ile Thr Arg Asp Arg Pro Val Arg Ala Leu Ala Glu Ala Ser Glu Asn
 245 250 255

Ala Gln Leu Leu Val Val Gly Ser His Gly Arg Gly Gly Phe Lys Gly
 260 265 270

Met Leu Leu Gly Ser Thr Ser Arg Ala Leu Leu Gln Ser Ala Pro Cys
 275 280 285

Pro Met Met Val Val Arg Pro Pro Glu Lys Ile Lys Lys
 290 295 300

<210> 15
 <211> 1059
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (101)..(1036)
 <223> RXC00552

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gtttttaagg tagccacaca tcgcactaga ctgaagaact gtg gct acc tca aaa 115
 Val Ala Thr Ser Lys
 1 5

att ctt ctt tat tac gca ttc acc ccg ctc tct gac cct aaa gcg gtt 163
 Ile Leu Leu Tyr Tyr Ala Phe Thr Pro Leu Ser Asp Pro Lys Ala Val
 10 15 20

cag ctg tgg cag cgt gag ctc tgc gag tca ctg aat ctt cgt gcg cgc 211
 Gln Leu Trp Gln Arg Glu Leu Cys Glu Ser Leu Asn Leu Arg Gly Arg
 25 30 35

atc ctg atc tcc act cac ggc atc aat gga acc gtg ggc gga gat att 259
 Ile Leu Ile Ser Thr His Gly Ile Asn Gly Thr Val Gly Gly Asp Ile
 40 45 50

gat gat tgc aag gcg tac att aaa aag acc cgc gag tac cca ggt ttc 307
 Asp Asp Cys Lys Ala Tyr Ile Lys Lys Thr Arg Glu Tyr Pro Gly Phe
 55 60 65

aac cgc atg cag ttt aag tgg tcc gag ggt ggc gct gag gat ttc cca 355
 Asn Arg Met Gln Phe Lys Trp Ser Glu Gly Gly Ala Glu Asp Phe Pro
 70 75 80 85

aag ctc agt gtc aaa gtc cgc gat gag atc gtt gcc ttc ggc gct cca 403
 Lys Leu Ser Val Lys Val Arg Asp Glu Ile Val Ala Phe Gly Ala Pro
 90 95 100

gat gag ctc aaa gtg gat gaa aac ggc gtc gtc ggt ggc ggc gtt cac 451
 Asp Glu Leu Lys Val Asp Glu Asn Gly Val Val Gly Gly Gly Val His
 105 110 115

ctg aaa cca cag cag gtc aat gag ctt gtg gaa gcc cgt ggc gat gaa 499
 Leu Lys Pro Gln Gln Val Asn Glu Leu Val Glu Ala Arg Gly Asp Glu
 120 125 130

gtt gtg ttc ttt gac ggc cgc aac gca atg gaa gcc cag atc ggc aag 547
 Val Val Phe Phe Asp Gly Arg Asn Ala Met Glu Ala Gln Ile Gly Lys
 135 140 145

ttc aag gac gct gtt gtc cct gac gta gaa acc act cat gat ttc atc 595
 Phe Lys Asp Ala Val Val Pro Asp Val Glu Thr Thr His Asp Phe Ile
 150 155 160 165

gca gaa att gag tct gga aaa tac gac gat ctc aaa gac aag cct gtg 643
 Ala Glu Ile Glu Ser Gly Lys Tyr Asp Asp Leu Lys Asp Lys Pro Val
 170 175 180

gtc acc tac tgc acc ggc gga att cgt tgt gag atc ctg agt tca ctc 691
 Val Thr Tyr Cys Thr Gly Gly Ile Arg Cys Glu Ile Leu Ser Ser Leu
 185 190 195

atg atc aac cgt ggt ttc aaa gag gtc tac caa atc gat ggc ggc atc 739
 Met Ile Asn Arg Gly Phe Lys Glu Val Tyr Gln Ile Asp Gly Gly Ile
 200 205 210

gtt cgc tac ggc gag cag ttt ggc aac aag ggc ctg tgg gaa ggc tcc 787
 Val Arg Tyr Gly Glu Gln Phe Gly Asn Lys Gly Leu Trp Glu Gly Ser
 215 220 225

ctc tac gtt ttc gat aag cgc atg cat atg gaa ttc ggc gag gat tac 835
 Leu Tyr Val Phe Asp Lys Arg Met His Met Glu Phe Gly Glu Asp Tyr
 230 235 240 245

aaa gag gtc gga cac tgc atc cat tgc gat act ccc acc aac aaa ttt 883
 Lys Glu Val Gly His Cys Ile His Cys Asp Thr Pro Thr Asn Lys Phe
 250 255 260

gag cac tgc ctc aac gaa gat gat tgc cgc gag ctc gtg ttg atg tgc 931
 Glu His Cys Leu Asn Glu Asp Asp Cys Arg Glu Leu Val Leu Met Cys
 265 270 275

cct gat tgc ttc gcc aat gtt gag acc cgt cat tgc aag cgc gaa cgc 979
 Pro Asp Cys Phe Ala Asn Val Glu Thr Arg His Cys Lys Arg Glu Arg
 280 285 290

tgt gca gca att gct gcg gat ttc gct gag caa gga att gat ccg ctc
 1027
 Cys Ala Ala Ile Ala Ala Asp Phe Ala Glu Gln Gly Ile Asp Pro Leu
 295 300 305

gtt act tct taaaaagggt atggtggctg ggt
 1059
 Val Thr Ser
 310

<210> 16

<211> 312

<212> PRT

<213> Corynebacterium glutamicum

<400> 16

Val Ala Thr Ser Lys Ile Leu Leu Tyr Tyr Ala Phe Thr Pro Leu Ser
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Asp Pro Lys Ala Val Gln Leu Trp Gln Arg Glu Leu Cys Glu Ser Leu
 20 25 30

Asn Leu Arg Gly Arg Ile Leu Ile Ser Thr His Gly Ile Asn Gly Thr
 35 40 45

Val Gly Gly Asp Ile Asp Asp Cys Lys Ala Tyr Ile Lys Lys Thr Arg
 50 55 60

Glu Tyr Pro Gly Phe Asn Arg Met Gln Phe Lys Trp Ser Glu Gly Gly
 65 70 75 80
 Ala Glu Asp Phe Pro Lys Leu Ser Val Lys Val Arg Asp Glu Ile Val
 85 90 95
 Ala Phe Gly Ala Pro Asp Glu Leu Lys Val Asp Glu Asn Gly Val Val
 100 105 110
 Gly Gly Gly Val His Leu Lys Pro Gln Gln Val Asn Glu Leu Val Glu
 115 120 125
 Ala Arg Gly Asp Glu Val Val Phe Phe Asp Gly Arg Asn Ala Met Glu
 130 135 140
 Ala Gln Ile Gly Lys Phe Lys Asp Ala Val Val Pro Asp Val Glu Thr
 145 150 155 160
 Thr His Asp Phe Ile Ala Glu Ile Glu Ser Gly Lys Tyr Asp Asp Leu
 165 170 175
 Lys Asp Lys Pro Val Val Thr Tyr Cys Thr Gly Gly Ile Arg Cys Glu
 180 185 190
 Ile Leu Ser Ser Leu Met Ile Asn Arg Gly Phe Lys Glu Val Tyr Gln
 195 200 205
 Ile Asp Gly Gly Ile Val Arg Tyr Gly Glu Gln Phe Gly Asn Lys Gly
 210 215 220
 Leu Trp Glu Gly Ser Leu Tyr Val Phe Asp Lys Arg Met His Met Glu
 225 230 235 240
 Phe Gly Glu Asp Tyr Lys Glu Val Gly His Cys Ile His Cys Asp Thr
 245 250 255
 Pro Thr Asn Lys Phe Glu His Cys Leu Asn Glu Asp Asp Cys Arg Glu
 260 265 270
 Leu Val Leu Met Cys Pro Asp Cys Phe Ala Asn Val Glu Thr Arg His
 275 280 285
 Cys Lys Arg Glu Arg Cys Ala Ala Ile Ala Ala Asp Phe Ala Glu Gln
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 Gly Ile Asp Pro Leu Val Thr Ser
 305 310

<210> 17

<211> 1578

<212> DNA

<213> Corynebacterium glutamicum

<220>

<221> CDS

<222> (101)..(1555)

<223> RXN00351

<400> 17

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	Met Asp Asp Ser Asn	
	1 5	
agc ttt gta gtt gtt gct aac cgt ctg cca gtg gat atg act gtc cac	163	
Ser Phe Val Val Val Ala Asn Arg Leu Pro Val Asp Met Thr Val His		
10 15 20		
cca gat ggt agc tat agc atc tcc ccc agc ccc ggt ggc ctt gtc acg	211	
Pro Asp Gly Ser Tyr Ser Ile Ser Pro Ser Pro Gly Gly Leu Val Thr		
25 30 35		
ggg ctt tcc ccc gtt ctg gaa caa cat cgt gga tgt tgg gtc gga tgg	259	
Gly Leu Ser Pro Val Leu Glu Gln His Arg Gly Cys Trp Val Gly Trp		
40 45 50		
cct gga act gta gat gtt gca ccc gaa cca ttt cga aca gat acg ggt	307	
Pro Gly Thr Val Asp Val Ala Pro Glu Pro Phe Arg Thr Asp Thr Gly		
55 60 65		
gtt ttg ctg cac cct gtt gtc ctc act gca agt gac tat gaa ggc ttc	355	
Val Leu Leu His Pro Val Val Leu Thr Ala Ser Asp Tyr Glu Gly Phe		
70 75 80 85		
tac gag ggc ttt tca aac gca acg ctg tgg cct ctt ttc cac gat ctg	403	
Tyr Glu Gly Phe Ser Asn Ala Thr Leu Trp Pro Leu Phe His Asp Leu		
90 95 100		
att gtt act ccg gtg tac aac acc gat tgg tgg cat gcg ttt cgg gag	451	
Ile Val Thr Pro Val Tyr Asn Thr Asp Trp Trp His Ala Phe Arg Glu		
105 110 115		
gta aac ctc aag ttc gct gaa gcc gtg agc caa gtg gcg gca cac ggt	499	
Val Asn Leu Lys Phe Ala Glu Ala Val Ser Gln Val Ala Ala His Gly		
120 125 130		
gcc act gtg tgg gtg cag gac tat cag ctg ttg ctg gtt cct ggc att	547	
Ala Thr Val Trp Val Gln Asp Tyr Gln Leu Leu Leu Val Pro Gly Ile		
135 140 145		
ttg cgc cag atg cgc cct gat ttg aag atc ggt ttc ttc ctc cac att	595	
Leu Arg Gln Met Arg Pro Asp Leu Lys Ile Gly Phe Phe Leu His Ile		
150 155 160 165		
ccc ttc cct tcc cct gat ctg ttc cgt cag ctg ccg tgg cgt gaa gag	643	
Pro Phe Pro Ser Pro Asp Leu Phe Arg Gln Leu Pro Trp Arg Glu Glu		
170 175 180		
att gtt cga ggc atg ctg ggc gca gat ttg gtg gga ttc cat ttg gtt	691	
Ile Val Arg Gly Met Leu Gly Ala Asp Leu Val Gly Phe His Leu Val		
185 190 195		
caa aac gca gaa aac ttc ctt gcg tta acc cag cag gtt gcc ggc act	739	
Gln Asn Ala Glu Asn Phe Leu Ala Leu Thr Gln Gln Val Ala Gly Thr		
200 205 210		
gcc ggg tct cat gtg ggt cag ccg gac acc ttg cag gtc agt ggt gaa	787	
Ala Gly Ser His Val Gly Gln Pro Asp Thr Leu Gln Val Ser Gly Glu		
215 220 225		

gca ttg gtg cgt gag att ggc gct cat gtt gaa acc gct gac gga agg 835
 Ala Leu Val Arg Glu Ile Gly Ala His Val Glu Thr Ala Asp Gly Arg
 230 235 240 245

cga gtt agc gtc ggg gcg ttc ccg atc tcg att gat gtt gaa atg ttt 883
 Arg Val Ser Val Gly Ala Phe Pro Ile Ser Ile Asp Val Glu Met Phe
 250 255 260

ggg gag gcg tcg aaa agc gcc gtt ctt gat ctt tta aaa acg ctc gac 931
 Gly Glu Ala Ser Lys Ser Ala Val Leu Asp Leu Leu Lys Thr Leu Asp
 265 270 275

gag ccg gaa acc gta ttc ctg ggc gtt gac cga ctg gac tac acc aag 979
 Glu Pro Glu Thr Val Phe Leu Gly Val Asp Arg Leu Asp Tyr Thr Lys
 280 285 290

ggc att ttg cag cgc ctg ctt gcg ttt gag gaa ctg ctg gaa tcc ggc
 1027
 Gly Ile Leu Gln Arg Leu Leu Ala Phe Glu Glu Leu Leu Glu Ser Gly
 295 300 305

gcg ttg gag gcc gac aaa gct gtg ttg ctg cag gtc gcg acg cct tcg
 1075
 Ala Leu Glu Ala Asp Lys Ala Val Leu Leu Gln Val Ala Thr Pro Ser
 310 315 320 325

cgt gag cgc att gat cac tat cgt gtg tcg cgt tcg cag gtc gag gaa
 1123
 Arg Glu Arg Ile Asp His Tyr Arg Val Ser Arg Ser Gln Val Glu Glu
 330 335 340

gcc gtc ggc cgt atc aat ggt cgt ttc ggt cgc atg ggg cgt ccc gtg
 1171
 Ala Val Gly Arg Ile Asn Gly Arg Phe Gly Arg Met Gly Arg Pro Val
 345 350 355

gtg cat tat cta cac agg tca ttg agc aaa aat gat ctc cag gtg ctg
 1219
 Val His Tyr Leu His Arg Ser Leu Ser Lys Asn Asp Leu Gln Val Leu
 360 365 370

tat acc gca gcc gat gtc atg ctg gtt acg cct ttt aaa gac ggt atg
 1267
 Tyr Thr Ala Ala Asp Val Met Leu Val Thr Pro Phe Lys Asp Gly Met
 375 380 385

aac ttg gtg gct aaa gaa ttc gtg gcc aac cac cgc gac ggc act ggt
 1315
 Asn Leu Val Ala Lys Glu Phe Val Ala Asn His Arg Asp Gly Thr Gly
 390 395 400 405

gct ttg gtg ctg tcc gaa ttt gcc ggc gcg gcc act gag ctg acc ggt
 1363
 Ala Leu Val Leu Ser Glu Phe Ala Gly Ala Ala Thr Glu Leu Thr Gly
 410 415 420

gcg tat tta tgc aac cca ttt gat gtg gaa tcc atc aaa cgg caa atg
 1411
 Ala Tyr Leu Cys Asn Pro Phe Asp Val Glu Ser Ile Lys Arg Gln Met
 425 430 435

gtg gca gct gtc cat gat ttg aag cac aat ccg gaa tct gcg gca acg
1459

Val Ala Ala Val His Asp Leu Lys His Asn Pro Glu Ser Ala Ala Thr
440 445 450

cga atg aaa acg aac agc gag cag gtc tat acc cac gac gtc aac gtg
1507

Arg Met Lys Thr Asn Ser Glu Gln Val Tyr Thr His Asp Val Asn Val
455 460 465

ttg gct aat agt ttc ctg gat tgt ttg gca cag tcg gga gaa aac tca
1555

Trp Ala Asn Ser Phe Leu Asp Cys Leu Ala Gln Ser Gly Glu Asn Ser
470 475 480 485

tgaaccgcgc acgaatcgcg acc
1578

<210> 18

<211> 485

<212> PRT

<213> Corynebacterium glutamicum

<400> 18

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1 5 10 15

Asp Met Thr Val His Pro Asp Gly Ser Tyr Ser Ile Ser Pro Ser Pro
20 25 30

Gly Gly Leu Val Thr Gly Leu Ser Pro Val Leu Glu Gln His Arg Gly
35 40 45

Cys Trp Val Gly Trp Pro Gly Thr Val Asp Val Ala Pro Glu Pro Phe
50 55 60

Arg Thr Asp Thr Gly Val Leu Leu His Pro Val Val Leu Thr Ala Ser
65 70 75 80

Asp Tyr Glu Gly Phe Tyr Glu Gly Phe Ser Asn Ala Thr Leu Trp Pro
85 90 95

Leu Phe His Asp Leu Ile Val Thr Pro Val Tyr Asn Thr Asp Trp Trp
100 105 110

His Ala Phe Arg Glu Val Asn Leu Lys Phe Ala Glu Ala Val Ser Gln
115 120 125

Val Ala Ala His Gly Ala Thr Val Trp Val Gln Asp Tyr Gln Leu Leu
130 135 140

Leu Val Pro Gly Ile Leu Arg Gln Met Arg Pro Asp Leu Lys Ile Gly
145 150 155 160

Phe Phe Leu His Ile Pro Phe Pro Ser Pro Asp Leu Phe Arg Gln Leu
165 170 175

Pro Trp Arg Glu Ile Val Arg Gly Met Leu Gly Ala Asp Leu Val
180 185 190

Asp Val Ala Arg Gly Ala Gly Ala Asp Thr Val Gln Ile Ser Met Asp
 215 220 225
 caa gtc cgt gga aat gaa cat ttg gat ggt ttt ggt gaa acc atc acc 835
 Gln Val Arg Gly Asn Glu His Leu Asp Gly Phe Gly Glu Thr Ile Thr
 230 235 240 245
 agt gga att cgt ctt ggt ttg ggc att acg aca gga aaa gat gtc gta 883
 Ser Gly Ile Arg Leu Gly Leu Gly Ile Thr Thr Gly Lys Asp Val Val
 250 255 260
 gat gaa ctg ctc gag cga cgg cgg caa aag gcc gtt gag gta gca cgc 931
 Asp Glu Leu Leu Glu Arg Pro Arg Gln Lys Ala Val Glu Val Ala Arg
 265 270 275
 ttt ttt gat cgt tta ggt gtg ggc cga aac tat ctc gtg gat gct gtt 979
 Phe Phe Asp Arg Leu Gly Val Gly Arg Asn Tyr Leu Val Asp Ala Val
 280 285 290
 gat att cat cgg ggt gag gat ttg gtg cag ggg acc atc acc gag gcc
 1027
 Asp Ile His Pro Gly Glu Asp Leu Val Gln Gly Thr Ile Thr Glu Ala
 295 300 305
 ggg cag gct tat cgc atg gcc cgg gtg atg tcg gag atg ttg tcg aag
 1075
 Ala Gln Ala Tyr Arg Met Ala Arg Val Met Ser Glu Met Leu Ser Lys
 310 315 320 325
 gat tca tgc gac ctt taaggcttta ccggcgctgg gtg
 1113
 Asp Ser Cys Asp Leu
 330

<210> 202
 <211> 330
 <212> PRT
 <213> *Corynebacterium glutamicum*

<400> 202
 Leu Gly Ala Tyr Gly Leu Gly Glu Leu Pro Gly Lys Ser Ala Ala Glu
 1 5 10 15
 Ala Ala Asp Ile Ile Gln Gly Glu Thr Gly Asp Leu Leu His Ile Pro
 20 25 30
 Gln Leu Pro Ala Arg Gly Leu Gly Ala Asp Leu Ile Gly Arg Thr Val
 35 40 45
 Gly Leu Leu Asp Met Ile Asn Val Asp Arg Gly Ala Arg Ser Trp Val
 50 55 60
 Met Ser Thr Arg Pro Ser Arg Leu Thr His Leu Thr Gly Asp Phe Leu
 65 70 75 80
 Asp Met Asp Leu Asp Ala Cys Glu Glu Thr Trp Gly Thr Gly Val Asp
 85 90 95
 Lys Leu Lys Ile Gln Val Ala Gly Pro Trp Thr Leu Gly Ala Arg Ile
 100 105 110

Glu Leu Ala Asn Gly His Arg Val Leu Ser Asp Arg Gly Ala Met Arg
 115 120 125
 Asp Leu Thr Gln Ala Leu Ile Ala Gly Ile Asp Ala His Ala Arg Lys
 130 135 140
 Val Ala Gly Arg Phe Arg Ala Glu Val Gln Val Gln Ile Asp Glu Pro
 145 150 155 160
 Glu Leu Lys Ser Leu Ile Asp Gly Ser Leu Pro Gly Thr Ser Thr Phe
 165 170 175
 Asp Ile Ile Pro Ala Val Asn Val Ala Asp Ala Ser Glu Arg Leu Gln
 180 185 190
 Gln Val Phe Ser Ser Ile Glu Gly Pro Thr Tyr Leu Asn Leu Thr Gly
 195 200 205
 Gln Ile Pro Thr Trp Asp Val Ala Arg Gly Ala Gly Ala Asp Thr Val
 210 215 220
 Gln Ile Ser Met Asp Gln Val Arg Gly Asn Glu His Leu Asp Gly Phe
 225 230 235 240
 Gly Glu Thr Ile Thr Ser Gly Ile Arg Leu Gly Leu Gly Ile Thr Thr
 245 250 255
 Gly Lys Asp Val Val Asp Glu Leu Leu Glu Arg Pro Arg Gln Lys Ala
 260 265 270
 Val Glu Val Ala Arg Phe Phe Asp Arg Leu Gly Val Gly Arg Asn Tyr
 275 280 285
 Leu Val Asp Ala Val Asp Ile His Pro Gly Glu Asp Leu Val Gln Gly
 290 295 300
 Thr Ile Thr Glu Ala Ala Gln Ala Tyr Arg Met Ala Arg Val Met Ser
 305 310 315 320
 Glu Met Leu Ser Lys Asp Ser Cys Asp Leu
 325 330

<210> 203
 <211> 623
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (1)..(600)
 <223> RXN00402

<400> 203
 act gac gaa aag gat gga aag cca gta ttg ccc tac ttc gtc act cca 48
 Thr Asp Glu Lys Asp Gly Lys Pro Val Leu Pro Tyr Phe Val Thr Pro
 1 5 10 15
 gat gct gct tac cac gga ttg aag tac gca gac ctt ggt gca cca gcc 96
 Asp Ala Ala Tyr His Gly Leu Lys Tyr Ala Asp Leu Gly Ala Pro Ala

20	25	30	
ttc ggc ctc aag gtt cgc gtt ggc ctt cta cgc gac acc ggc tcc acc			144
Phe Gly Leu Lys Val Arg Val Gly Leu Leu Arg Asp Thr Gly Ser Thr			
35	40	45	
ctc tcc gca ttc aac gca tgg gct gca gtc cag ggc atc gac acc ctt			192
Leu Ser Ala Phe Asn Ala Trp Ala Ala Val Gln Gly Ile Asp Thr Leu			
50	55	60	
tcc ctg cgc ctg gag cgc cac aac gaa aac gcc atc aag gtt gca gaa			240
Ser Leu Arg Leu Glu Arg His Asn Glu Asn Ala Ile Lys Val Ala Glu			
65	70	75	80
ttc ctc aac aac cac gag aag gtg gaa aag gtt aac ttc gca ggc ctg			288
Phe Leu Asn Asn His Glu Lys Val Glu Lys Val Asn Phe Ala Gly Leu			
85	90	95	
aag gat tcc cct tgg tac gca acc aag gaa aag ctt ggc ctg aag tac			336
Lys Asp Ser Pro Trp Tyr Ala Thr Lys Glu Lys Leu Gly Leu Lys Tyr			
100	105	110	
acc ggc tcc gtt ctc acc ttc gag atc aag ggc ggc aag gat gag gct			384
Thr Gly Ser Val Leu Thr Phe Glu Ile Lys Gly Gly Lys Asp Glu Ala			
115	120	125	
tgg gca ttt atc gac gcc ctg aag cta cac tcc aac ctt gca aac atc			432
Trp Ala Phe Ile Asp Ala Leu Lys Leu His Ser Asn Leu Ala Asn Ile			
130	135	140	
ggc gat gtt cgc tcc ctc gtt gtt cac cca gca acc acc acc cat tca			480
Gly Asp Val Arg Ser Leu Val Val His Pro Ala Thr Thr Thr His Ser			
145	150	155	160
cag tcc gac gaa gct ggc ctg gca cgc gcg ggc gtt acc cag tcc acc			528
Gln Ser Asp Glu Gly Leu Ala Arg Ala Gly Val Thr Gln Ser Thr			
165	170	175	
gtc cgc ctg tcc gtt ggc atc gag acc att gat gat atc atc gct gac			576
Val Arg Leu Ser Val Gly Ile Glu Thr Ile Asp Asp Ile Ile Ala Asp			
180	185	190	
ctc gaa ggc ggc ttt gct gca atc tagctttaaa tagactcacc cca			623
Leu Glu Gly Gly Phe Ala Ala Ile			
195	200		

<210> 204

<211> 200

<212> FRT

<213> Corynebacterium glutamicum

<400> 204

Thr Asp Glu Lys Asp Gly Lys Pro Val Leu Pro Tyr Phe Val Thr Pro
 1 5 10 15

Asp Ala Ala Tyr His Gly Leu Lys Tyr Ala Asp Leu Gly Ala Pro Ala
 20 25 30

Phe Gly Leu Lys Val Arg Val Gly Leu Leu Arg Asp Thr Gly Ser Thr
 35 40 45

Leu Ser Ala Phe Asn Ala Trp Ala Ala Val Gln Gly Ile Asp Thr Leu
 50 55 60
 Ser Leu Arg Leu Glu Arg His Asn Glu Asn Ala Ile Lys Val Ala Glu
 65 70 75 80
 Phe Leu Asn Asn His Glu Lys Val Glu Lys Val Asn Phe Ala Gly Leu
 85 90 95
 Lys Asp Ser Pro Trp Tyr Ala Thr Lys Glu Lys Leu Gly Leu Lys Tyr
 100 105 110
 Thr Gly Ser Val Leu Thr Phe Glu Ile Lys Gly Gly Lys Asp Glu Ala
 115 120 125
 Trp Ala Phe Ile Asp Ala Leu Lys Leu His Ser Asn Leu Ala Asn Ile
 130 135 140
 Gly Asp Val Arg Ser Leu Val Val His Pro Ala Thr Thr Thr His Ser
 145 150 155 160
 Gln Ser Asp Glu Ala Gly Leu Ala Arg Ala Gly Val Thr Gln Ser Thr
 165 170 175
 Val Arg Leu Ser Val Gly Ile Glu Thr Ile Asp Asp Ile Ile Ala Asp
 180 185 190
 Leu Glu Gly Gly Phe Ala Ala Ile
 195 200

<210> 205
 <211> 599
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (1)..(576)
 <223> FRXA00402

<400> 205
 gta ttg ccc tac ttc gtc act cca gat gct gct tac cac gga ttg aag 48
 Val Leu Pro Tyr Phe Val Thr Pro Asp Ala Ala Tyr His Gly Leu Lys
 1 5 10 15
 tac gca gac ctt ggt gca cca gcc ttc ggc ctc aag gtt cgc gtt ggc 96
 Tyr Ala Asp Leu Gly Ala Pro Ala Phe Gly Leu Lys Val Arg Val Gly
 20 25 30
 ctt cta cgc gac acc ggc tcc acc ctc tcc gca ttc aac gca tgg gct 144
 Leu Leu Arg Asp Thr Gly Ser Thr Leu Ser Ala Phe Asn Ala Trp Ala
 35 40 45
 gca gtc cag ggc atc gac acc ctt tcc ctg cgc ctg gag cgc cac aac 192
 Ala Val Gln Gly Ile Asp Thr Leu Ser Leu Arg Leu Glu Arg His Asn
 50 55 60
 gaa aac gcc atc aag gtt gca gaa ttc ctc aac aac cac gag aag gtg 240
 Glu Asn Ala Ile Lys Val Ala Glu Phe Leu Asn Asn His Glu Lys Val

65	70	75	80	
gaa aag gtt aac ttc gca ggc ctg aag gat tcc cct tgg tac gca acc				288
Glu Lys Val Asn Phe Ala Gly Leu Lys Asp Ser Pro Trp Tyr Ala Thr				
	85	90	95	
aag gaa aag ctt ggc ctg aag tac acc ggc tcc gtt ctc acc ttc gag				336
Lys Glu Lys Leu Gly Leu Lys Tyr Thr Gly Ser Val Leu Thr Phe Glu				
	100	105	110	
atc aag ggc ggc aag gat gag gct tgg gca ttt atc gac gcc ctg aag				384
Ile Lys Gly Gly Lys Asp Glu Ala Trp Ala Phe Ile Asp Ala Leu Lys				
	115	120	125	
cta cac tcc aac ctt gca aac atc ggc gat gtt cgc tcc ctc gtt gtt				432
Leu His Ser Asn Leu Ala Asn Ile Gly Asp Val Arg Ser Leu Val Val				
	130	135	140	
cac cca gca acc acc acc cat tca cag tcc gac gaa gct ggc ctg gca				480
His Pro Ala Thr Thr Thr His Ser Gln Ser Asp Glu Ala Gly Leu Ala				
	145	150	155	160
cgc ggc ggc gtt acc cag tcc acc gtc cgc ctg tcc gtt ggc atc gag				528
Arg Ala Gly Val Thr Gln Ser Thr Val Arg Leu Ser Val Gly Ile Glu				
	165	170	175	
acc att gat gat atc atc gct gac ctc gaa ggc ggc ttt gct gca atc				576
Thr Ile Asp Asp Ile Ile Ala Asp Leu Glu Gly Gly Phe Ala Ala Ile				
	180	185	190	
tagctttaaa tagactcacc cca				599

<210> 206

<211> 192

<212> PRT

<213> Corynebacterium glutamicum

<400> 206

Val	Leu	Pro	Tyr	Phe	Val	Thr	Pro	Asp	Ala	Ala	Tyr	His	Gly	Leu	Lys
1					5				10					15	

Tyr	Ala	Asp	Leu	Gly	Ala	Pro	Ala	Phe	Gly	Leu	Lys	Val	Arg	Val	Gly
			20					25					30		

Leu	Leu	Arg	Asp	Thr	Gly	Ser	Thr	Leu	Ser	Ala	Phe	Asn	Ala	Trp	Ala
		35					40					45			

Ala	Val	Gln	Gly	Ile	Asp	Thr	Leu	Ser	Leu	Arg	Leu	Glu	Arg	His	Asn
	50					55					60				

Glu	Asn	Ala	Ile	Lys	Val	Ala	Glu	Phe	Leu	Asn	Asn	His	Glu	Lys	Val
	65				70					75				80	

Glu	Lys	Val	Asn	Phe	Ala	Gly	Leu	Lys	Asp	Ser	Pro	Trp	Tyr	Ala	Thr
			85						90					95	

Lys	Glu	Lys	Leu	Gly	Leu	Lys	Tyr	Thr	Gly	Ser	Val	Leu	Thr	Phe	Glu
			100				105						110		

Ile	Lys	Gly	Gly	Lys	Asp	Glu	Ala	Trp	Ala	Phe	Ile	Asp	Ala	Leu	Lys
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

115	120	125
Leu His Ser Asn Leu Ala Asn Ile Gly Asp Val Arg Ser Leu Val Val		
130	135	140
His Pro Ala Thr Thr Thr His Ser Gln Ser Asp Glu Ala Gly Leu Ala		
145	150	155
		160
Arg Ala Gly Val Thr Gln Ser Thr Val Arg Leu Ser Val Gly Ile Glu		
	165	170
		175
Thr Ile Asp Asp Ile Ile Ala Asp Leu Glu Gly Gly Phe Ala Ala Ile		
180	185	190

<210> 207
 <211> 613
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (101)..(613)
 <223> RXA00405

<400> 207
 agaataaatt tataccacac agtctattgc aatagaccaa gctgttcagt aggggtgcatg 60

ggagaagaat ttctaataa aaactcttaa ggacctcaa atg cca aag tac gac 115
 Met Pro Lys Tyr Asp
 1 5

aat tcc aat gct gac cag tgg ggc ttt gaa acc cgc tcc att cac gca 163
 Asn Ser Asn Ala Asp Gln Trp Gly Phe Glu Thr Arg Ser Ile His Ala
 10 15 20

ggc cag tca gta gac gca cag acc agc gca cga aac ctt ccg atc tac 211
 Gly Gln Ser Val Asp Ala Gln Thr Ser Ala Arg Asn Leu Pro Ile Tyr
 25 30 35

caa tcc acc gct ttc gtg ttc gac tcc gct gag cac gcc aag cag cgt 259
 Gln Ser Thr Ala Phe Val Phe Asp Ser Ala Glu His Ala Lys Gln Arg
 40 45 50

ttc gca ctt gag gat cta ggc cct gtt tac tcc cgc ctc acc aac cca 307
 Phe Ala Leu Glu Asp Leu Gly Pro Val Tyr Ser Arg Leu Thr Asn Pro
 55 60 65

acc gtt gag gct ttg gaa aac cgc atc gct tcc ctc gaa ggt ggc gtc 355
 Thr Val Glu Ala Leu Glu Asn Arg Ile Ala Ser Leu Glu Gly Gly Val
 70 75 80 85

cac gct gta gcg ttc tcc tcc gga cag gcc gca acc acc aac gcc att 403
 His Ala Val Ala Phe Ser Ser Gly Gln Ala Ala Thr Thr Asn Ala Ile
 90 95 100

ttg aac ctg gca gga gcg ggc gac cac atc gtc acc tcc cca cgc ctc 451
 Leu Asn Leu Ala Gly Ala Gly Asp His Ile Val Thr Ser Pro Arg Leu

105	110	115	
tac ggt ggc acc gag act eta ttc ctt atc act ctt aac cgc ctg ggt			499
Tyr Gly Gly Thr Glu Thr Leu Phe Leu Ile Thr Leu Asn Arg Leu Gly			
120	125	130	
atc gat gtt tcc ttc gtg gaa aac ccc gac gac cct gag tcc tgg cag			547
Ile Asp Val Ser Phe Val Glu Asn Pro Asp Asp Pro Glu Ser Trp Gln			
135	140	145	
gca gcc gtt cag cca aac acc aaa gca ttc ttc ggc gag act ttc gcc			595
Ala Ala Val Gln Pro Asn Thr Lys Ala Phe Phe Gly Glu Thr Phe Ala			
150	155	160	165
aac cca cag gca gac gtc			613
Asn Pro Gln Ala Asp Val			
170			

<210> 208

<211> 171

<212> PRT

<213> Corynebacterium glutamicum

<400> 208

Met Pro Lys Tyr Asp Asn Ser Asn Ala Asp Gln Trp Gly Phe Glu Thr			
1	5	10	15
Arg Ser Ile His Ala Gly Gln Ser Val Asp Ala Gln Thr Ser Ala Arg			
20	25	30	
Asn Leu Pro Ile Tyr Gln Ser Thr Ala Phe Val Phe Asp Ser Ala Glu			
35	40	45	
His Ala Lys Gln Arg Phe Ala Leu Glu Asp Leu Gly Pro Val Tyr Ser			
50	55	60	
Arg Leu Thr Asn Pro Thr Val Glu Ala Leu Glu Asn Arg Ile Ala Ser			
65	70	75	80
Leu Glu Gly Gly Val His Ala Val Ala Phe Ser Ser Gly Gln Ala Ala			
85	90	95	
Thr Thr Asn Ala Ile Leu Asn Leu Ala Gly Ala Gly Asp His Ile Val			
100	105	110	
Thr Ser Pro Arg Leu Tyr Gly Gly Thr Glu Thr Leu Phe Leu Ile Thr			
115	120	125	
Leu Asn Arg Leu Gly Ile Asp Val Ser Phe Val Glu Asn Pro Asp Asp			
130	135	140	
Pro Glu Ser Trp Gln Ala Ala Val Gln Pro Asn Thr Lys Ala Phe Phe			
145	150	155	160
Gly Glu Thr Phe Ala Asn Pro Gln Ala Asp Val			
165	170		

<210> 209

<211> 551

<212> DNA

<213> Corynebacterium glutamicum

<220>

<221> CDS

<222> (1)..(528)

<223> RXA02197

<400> 209

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gcc gaa cgc atg cgc ttt agc ttc cca cgc cag cag cgc ggc agg ttc   48
Ala Glu Arg Met Arg Phe Ser Phe Pro Arg Gln Gln Arg Gly Arg Phe
  1             5             10             15

```

```

ttg tgc atc gcg gat ttc att cgc cca cgc gag caa gct gtc aag gac   96
Leu Cys Ile Ala Asp Phe Ile Arg Pro Arg Glu Gln Ala Val Lys Asp
          20             25             30

```

```

ggc caa gtg gac gtc atg cca ttc cag ctg gtc acc atg ggt aat cct   144
Gly Gln Val Asp Val Met Pro Phe Gln Leu Val Thr Met Gly Asn Pro
          35             40             45

```

```

att gct gat ttc gcc aac gag ttg ttc gca gcc aat gaa tac cgc gag   192
Ile Ala Asp Phe Ala Asn Glu Leu Phe Ala Ala Asn Glu Tyr Arg Glu
          50             55             60

```

```

tac ttg gaa gtt cac ggc atc ggc gtg cag ctc acc gaa gca ttg gcc   240
Tyr Leu Glu Val His Gly Ile Gly Val Gln Leu Thr Glu Ala Leu Ala
          65             70             75             80

```

```

gag tac tgg cac tcc cga gtg cgc agc gaa ctc aag ctg aac gac ggt   288
Glu Tyr Trp His Ser Arg Val Arg Ser Glu Leu Lys Leu Asn Asp Gly
          85             90             95

```

```

gga tct gtc gct gat ttt gat cca gaa gac aag acc aag ttc ttc gac   336
Gly Ser Val Ala Asp Phe Asp Pro Glu Asp Lys Thr Lys Phe Phe Asp
          100             105             110

```

```

ctg gat tac cgc ggc gcc cgc ttc tcc ttt ggt tac ggt tct tgc cct   384
Leu Asp Tyr Arg Gly Ala Arg Phe Ser Phe Gly Tyr Gly Ser Cys Pro
          115             120             125

```

```

gat ctg gaa gac cgc gca aag ctg gtg gaa ttg ctc gag cca ggc cgt   432
Asp Leu Glu Asp Arg Ala Lys Leu Val Glu Leu Leu Glu Pro Gly Arg
          130             135             140

```

```

atc ggc gtg gag ttg tcc gag gaa ctc cag ctg cac cca gag cag tcc   480
Ile Gly Val Glu Leu Ser Glu Glu Leu Gln Leu His Pro Glu Gln Ser
          145             150             155             160

```

```

aca gac gcg ttt gtg ctc tac cac cca gag gca aag tac ttt aac gtc   528
Thr Asp Ala Phe Val Leu Tyr His Pro Glu Ala Lys Tyr Phe Asn Val
          165             170             175

```

```

taacaccttt gagaggaaa act   551

```

<210> 210

<211> 176

<212> PRT

<213> Corynebacterium glutamicum

Lys Ala Asp Glu Ile Val Ala Glu Arg Glu Asn Ala Val Leu Ala Arg
 130 135 140
 Gln Phe Glu Asn Glu Ala Asn Pro Arg Val Asn Arg Asp Thr Thr Ala
 145 150 155 160
 Lys Glu Ile Leu Glu Asp Thr Asp Gly Thr Val Asp Ile Phe Val Ala
 165 170 175
 Ser Phe Gly Thr Gly Gly Thr Val Thr Gly Val Gly Gln Val Leu Lys
 180 185 190
 Glu Asn Asn Ala Asp Val Gln Val Tyr Thr Val Glu Pro Glu Ala Ser
 195 200 205
 Pro Leu Leu Thr Ala Gly Lys Ala Gly Pro His Lys Ile Gln Gly Ile
 210 215 220
 Gly Ala Asn Phe Ile Pro Glu Val Leu Asp Arg Lys Val Leu Asp Asp
 225 230 235 240
 Val Leu Thr Val Ser Asn Glu Asp Ala Ile Ala Phe Ser Arg Lys Leu
 245 250 255
 Ala Thr Glu Glu Gly Ile Leu Gly Gly Ile Ser Thr Gly Ala Asn Ile
 260 265 270
 Lys Ala Ala Leu Asp Leu Ala Ala Lys Pro Glu Asn Ala Gly Lys Thr
 275 280 285
 Ile Val Thr Val Val Thr Asp Phe Gly Glu Arg Tyr Val Ser Thr Val
 290 295 300
 Leu Tyr Glu Asp Ile Arg Asp
 305 310

<210> 247
 <211> 623
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (1)..(600)
 <223> RXN00402

<400> 247
 act gac gaa aag gat gga aag cca gta ttg ccc tac ttc gtc act cca 48
 Thr Asp Glu Lys Asp Gly Lys Pro Val Leu Pro Tyr Phe Val Thr Pro
 1 5 10 15
 gat gct gct tac cac gga ttg aag tac gca gac ctt ggt gca cca gcc 96
 Asp Ala Ala Tyr His Gly Leu Lys Tyr Ala Asp Leu Gly Ala Pro Ala
 20 25 30
 ttc ggc ctc aag gtt cgc gtt ggc ctt cta cgc gac acc ggc tcc acc 144
 Phe Gly Leu Lys Val Arg Val Gly Leu Leu Arg Asp Thr Gly Ser Thr
 35 40 45
 ctc tcc gca ttc aac gca tgg gct gca gtc cag ggc atc gac acc ctt 192

Leu Ser Ala Phe Asn Ala Trp Ala Ala Val Gln Gly Ile Asp Thr Leu
 50 55 60
 tcc ctg cgc ctg gag cgc cac aac gaa aac gcc atc aag gtt gca gaa 240
 Ser Leu Arg Leu Glu Arg His Asn Glu Asn Ala Ile Lys Val Ala Glu
 65 70 75 80
 ttc ctc aac aac cac gag aag gtg gaa aag gtt aac ttc gca ggc ctg 288
 Phe Leu Asn Asn His Glu Lys Val Glu Lys Val Asn Phe Ala Gly Leu
 85 90 95
 aag gat tcc cct tgg tac gca acc aag gaa aag ctt ggc ctg aag tac 336
 Lys Asp Ser Pro Trp Tyr Ala Thr Lys Glu Lys Leu Gly Leu Lys Tyr
 100 105 110
 acc ggc tcc gtt ctc acc ttc gag atc aag ggc ggc aag gat gag gct 384
 Thr Gly Ser Val Leu Thr Phe Glu Ile Lys Gly Gly Lys Asp Glu Ala
 115 120 125
 tgg gca ttt atc gac gcc ctg aag cta cac tcc aac ctt gca aac atc 432
 Trp Ala Phe Ile Asp Ala Leu Lys Leu His Ser Asn Leu Ala Asn Ile
 130 135 140
 ggc gat gtt cgc tcc ctc gtt gtt cac cca gca acc acc acc cat tca 480
 Gly Asp Val Arg Ser Leu Val Val His Pro Ala Thr Thr Thr His Ser
 145 150 155 160
 cag tcc gac gaa gct ggc ctg gca cgc gcg ggc gtt acc cag tcc acc 528
 Gln Ser Asp Glu Ala Gly Leu Ala Arg Ala Gly Val Thr Gln Ser Thr
 165 170 175
 gtc cgc ctg tcc gtt ggc atc gag acc att gat gat atc atc gct gac 576
 Val Arg Leu Ser Val Gly Ile Glu Thr Ile Asp Asp Ile Ile Ala Asp
 180 185 190
 ctc gaa ggc ggc ttt gct gca atc tagctttaaa tagactcacc cca 623
 Leu Glu Gly Gly Phe Ala Ala Ile
 195 200

<210> 248

<211> 200

<212> PRT

<213> Corynebacterium glutamicum

<400> 248

Thr Asp Glu Lys Asp Gly Lys Pro Val Leu Pro Tyr Phe Val Thr Pro
 1 5 10 15
 Asp Ala Ala Tyr His Gly Leu Lys Tyr Ala Asp Leu Gly Ala Pro Ala
 20 25 30
 Phe Gly Leu Lys Val Arg Val Gly Leu Leu Arg Asp Thr Gly Ser Thr
 35 40 45
 Leu Ser Ala Phe Asn Ala Trp Ala Ala Val Gln Gly Ile Asp Thr Leu
 50 55 60
 Ser Leu Arg Leu Glu Arg His Asn Glu Asn Ala Ile Lys Val Ala Glu
 65 70 75 80

Phe Leu Asn Asn His Glu Lys Val Glu Lys Val Asn Phe Ala Gly Leu
 85 90 95
 Lys Asp Ser Pro Trp Tyr Ala Thr Lys Glu Lys Leu Gly Leu Lys Tyr
 100 105 110
 Thr Gly Ser Val Leu Thr Phe Glu Ile Lys Gly Gly Lys Asp Glu Ala
 115 120 125
 Trp Ala Phe Ile Asp Ala Leu Lys Leu His Ser Asn Leu Ala Asn Ile
 130 135 140
 Gly Asp Val Arg Ser Leu Val Val His Pro Ala Thr Thr Thr His Ser
 145 150 155 160
 Gln Ser Asp Glu Ala Gly Leu Ala Arg Ala Gly Val Thr Gln Ser Thr
 165 170 175
 Val Arg Leu Ser Val Gly Ile Glu Thr Ile Asp Asp Ile Ile Ala Asp
 180 185 190
 Leu Glu Gly Gly Phe Ala Ala Ile
 195 200

<210> 249
 <211> 599
 <212> DNA
 <213> Corynebacterium glutamicum

<220>
 <221> CDS
 <222> (1)..(576)
 <223> FRXA00402

<400> 249
 gta ttg ccc tac ttc gtc act cca gat gct gct tac cac gga ttg aag 48
 Val Leu Pro Tyr Phe Val Thr Pro Asp Ala Ala Tyr His Gly Leu Lys
 1 5 10 15
 tac gca gac ctt ggt gca cca gcc ttc ggc ctc aag gtt cgc gtt ggc 96
 Tyr Ala Asp Leu Gly Ala Pro Ala Phe Gly Leu Lys Val Arg Val Gly
 20 25 30
 ctt cta cgc gac acc ggc tcc acc ctc tcc gca ttc aac gca tgg gct 144
 Leu Leu Arg Asp Thr Gly Ser Thr Leu Ser Ala Phe Asn Ala Trp Ala
 35 40 45
 gca gtc cag ggc atc gac acc ctt tcc ctg cgc ctg gag cgc cac aac 192
 Ala Val Gln Gly Ile Asp Thr Leu Ser Leu Arg Leu Glu Arg His Asn
 50 55 60
 gaa aac gcc atc aag gtt gca gaa ttc ctc aac aac cac gag aag gtg 240
 Glu Asn Ala Ile Lys Val Ala Glu Phe Leu Asn Asn His Glu Lys Val
 65 70 75 80
 gaa aag gtt aac ttc gca ggc ctg aag gat tcc cct tgg tac gca acc 288
 Glu Lys Val Asn Phe Ala Gly Leu Lys Asp Ser Pro Trp Tyr Ala Thr
 85 90 95
 aag gaa aag ctt ggc ctg aag tac acc ggc tcc gtt ctc acc ttc gag 336

Lys Glu Lys Leu Gly Leu Lys Tyr Thr Gly Ser Val Leu Thr Phe Glu
 100 105 110
 atc aag ggc ggc aag gat gag gct tgg gca ttt atc gac gcc ctg aag 384
 ile lys gly gly lys asp glu ala trp ala phe ile asp ala leu lys
 115 120 125
 cta cac tcc aac ctt gca aac atc ggc gat gtt cgc tcc ctc gtt gtt 432
 leu his ser asn leu ala asn ile gly asp val arg ser leu val val
 130 135 140
 cac cca gca acc acc acc cat tca cag tcc gac gaa gct ggc ctg gca 480
 his pro ala thr thr thr his ser gln ser asp glu ala gly leu ala
 145 150 155 160
 cgc ggc ggc gtt acc cag tcc acc gtc cgc ctg tcc gtt ggc atc gag 528
 arg ala gly val thr gln ser thr val arg leu ser val gly ile glu
 165 170 175
 acc att gat gat atc atc gct gac ctc gaa ggc ggc ttt gct gca atc 576
 thr ile asp asp ile ile ala asp leu glu gly gly phe ala ala ile
 180 185 190
 tagctttaaa tagactcacc cca 599

<210> 250
 <211> 192
 <212> PRT
 <213> Corynebacterium glutamicum

<400> 250
 Val Leu Pro Tyr Phe Val Thr Pro Asp Ala Ala Tyr His Gly Leu Lys
 1 5 10 15
 Tyr Ala Asp Leu Gly Ala Pro Ala Phe Gly Leu Lys Val Arg Val Gly
 20 25 30
 Leu Leu Arg Asp Thr Gly Ser Thr Leu Ser Ala Phe Asn Ala Trp Ala
 35 40 45
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 Glu Lys Val Asn Phe Ala Gly Leu Lys Asp Ser Pro Trp Tyr Ala Thr
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 Lys Glu Lys Leu Gly Leu Lys Tyr Thr Gly Ser Val Leu Thr Phe Glu
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 His Pro Ala Thr Thr Thr His Ser Gln Ser Asp Glu Ala Gly Leu Ala
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 Gln Ser Thr Ala Phe Val Phe Asp Ser Ala Glu His Ala Lys Gln Arg
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 Phe Ala Leu Glu Asp Leu Gly Pro Val Tyr Ser Arg Leu Thr Asn Pro
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 Thr Val Glu Ala Leu Glu Asn Arg Ile Ala Ser Leu Glu Gly Gly Val
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 His Ala Val Ala Phe Ser Ser Gly Gln Ala Ala Thr Thr Asn Ala Ile
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 Tyr Gly Gly Thr Glu Thr Leu Phe Leu Ile Thr Leu Asn Arg Leu Gly
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Ile Asp Val Ser Phe Val Glu Asn Pro Asp Asp Pro Glu Ser Trp Gln
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